BUREAU OF HYGIENE AND TROPICAL DISEASES

TROPICAL DISEASES BULLETIN

Vol. 53] 1956 [No. 7

TREATMENT OF FILARIASIS

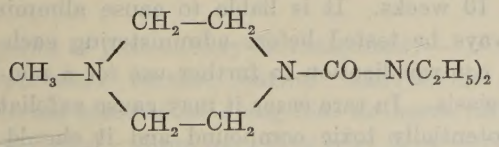
by

F. Hawking, D.M., M.R.C.P., D.T.M.

National Institute for Medical Research, London, N.W.7.

Filariasis is a state of infection by certain worms. Drugs are now available to kill many of the filarial worms which may occur in man. Their death may be expected to relieve symptoms which are directly due to the continued presence of the adult worms or of microfilariae, *e.g.*, Calabar swellings, or dermatitis due to microfilariae of *Onchocerca volvulus*. It will probably have no effect upon those other symptoms which are due to permanent after-effects of the worms, *e.g.*, elephantiasis due to fibrosis of lymphatics resulting from lymphangitis.

Treatment may be directed to curing the symptoms and infections of particular patients (individual therapy) or to sterilizing all the carriers of the infection in a certain area so that no more persons will become infected in future (prophylaxis by mass therapy, or attempted eradication). Two compounds are now established as being suitable for killing the filarial worms in man.



The first is diethylcarbamazine (Hetrazan, Banocide, Notézine, Caricide, Carbilazine, 3,799 R.P.). This is issued as the dihydrogencitrate which is acid and which contains only half of its weight as base. The dose is usually recorded in terms of the complete salt, and this usage is now too firmly established to be broken, although dosage in terms of the base would have been preferable. Doses are given below in terms of the salt.

It is administered by mouth and is rapidly absorbed. It is partially metabolized in the body, the side chains being degraded, and it is excreted in various forms in the urine within 1–2 days. It may have a slight direct toxic action—anorexia, nausea, vomiting and sleepiness—and in patients with filariasis it may cause various allergic reactions (for which see below). But it is an extremely safe compound, and although it has been administered widely, no fatal complication, *e.g.*, agranulocytosis, aplastic anaemia or exfoliative dermatitis, has ever been reported. The dose usually recommended is about 2 mgm. per kgm. 3 times a day, but single doses of 40 mgm. per kgm. have been given without ill effects worse than vomiting. Doses as low as 0·1 mgm. per kgm. will clear the blood of microfilariae (*Wuchereria bancrofti*) in some patients. This compound has a remarkably rapid action in destroying all kinds of microfilariae (except those of *Dipetalonema perstans* and *Mansonella*). As regards the adult worms, it is effective with *Loa loa*.

When it is given in adequate courses to patients with *W. bancrofti* or *W. malayi* the microfilariae disappear and usually they do not return even during a follow up of several years; accordingly it may be concluded that the adult female worms have been killed or (less probably) permanently sterilized. In the case of *Onchocerca volvulus*, the microfilariae are quickly killed but the adult worms are unaffected or only slightly affected, so that microfilariae soon reappear. Microfilariae of *D. perstans* usually appear unaffected by the drug, but there is evidence that a standard course of treatment will produce a permanent slight reduction in the number of microfilariae present, perhaps by killing a few of the adult worms. The microfilariae of *Mansonella ozzardi* are not affected by it, but those of *Tetrapetalonema streptocerca* disappear rapidly from the skin when it is given. *Dracunculus medinensis* is sensitive during its developmental stages.

The second compound is suramin (Antrypol, Bayer 205, Germanin, Moranyl, Naphuride, etc.) which is well known for the treatment of human trypanosomiasis. It is usually effective in killing the adult worms of *Onchocerca volvulus* and the microfilariae disappear gradually. Its action on the other human filarial infections is negligible. It is usually given intravenously in doses of 1 gm. for an adult of 50–70 kgm. once weekly for 5 or 10 weeks. It is liable to cause albuminuria, and the urine should always be tested before administering each dose; marked albuminuria is a contraindication to further use for a non-fatal condition such as onchocerciasis. In rare cases it may cause exfoliative dermatitis. Suramin is a potentially toxic compound and it should be used with discretion and restraint.

Other compounds have been described for the treatment of filariasis, but they are ineffective or too toxic. Arsenamide (thioglycollate derivative of $OAs.C_6H_5.CONH_2$) kills the adult worms, and less readily, the microfilariae of *W. bancrofti*, but it has a toxic action on the liver and one case of fatal necrosis of the liver has been reported after three

injections. It is too dangerous to use for treatment of a non-fatal infection. It is not effective in killing the adult worms of *Onchocerca*. Pentavalent antimonials, *e.g.*, Neostibosan, sometimes kill the adult worms of *W. bancrofti*, but they are too uncertain and too toxic for practical use. Other compounds, *e.g.*, cyanine 863, are toxic and ineffective. Further details about all these compounds may be found in a recent review by the present author (Hawking, 1955).

Infections by *W. bancrofti* and *W. malayi*.

These respond well to diethylcarbamazine.

Therapy of Individual Patients

For individual patients who can be trusted to take tablets as instructed, the best course of treatment is probably 100 mgm. by mouth 3 times a day for 10 days. If preferred, the course can be extended to 21 days; but it is really better to give the shorter course, to examine the blood a few days later, and if the microfilariae have not completely disappeared to give a second course after an interval of several weeks. The drug can also be given as a single dose of 200 or 300 mgm. once daily, if this is preferable for administrative reasons, but there is more tendency to cause gastro-intestinal upsets. Diethylcarbamazine may cause certain direct minor toxic effects, *viz.*, anorexia, nausea, vomiting, headache, sleepiness, but these are seldom of much importance. It may also cause allergic reactions due to the destruction of the microfilariae and of the adult worms, *e.g.*, pyrexia with cough and pain in the chest lasting 1–2 days, cutaneous eruptions, and localized painful swellings which may represent inflammation round a recently killed worm. All subside in a few days. Their incidence varies in different parts of the world, being much more marked in Malaya than in East Africa. They are seldom of importance in individual therapy, although they may hinder the acceptance of the drug during mass campaigns. Administration of antihistamine drugs or of calcium gluconate to prevent or diminish allergic reactions is not very effective and it is not worth while, except perhaps with heavy infections of *Onchocerca* where the allergic reactions may be violent.

Various categories of patient may be recognized:—

(i) *The symptomless carrier, having microfilariae in the blood.* Although the worms seem to be doing him no harm, they are certainly not doing him any good. Moreover, they may be a focus of infection to his neighbours. Accordingly he should be treated as above. Although rare patients may develop elephantiasis some time after treatment, this complication is less probable than it would have been if the patient had been left untreated.

(ii) *The patient with attacks of lymphangitis (and usually with microfilariae as well).* He should certainly be given diethylcarbamazine, since

treatment will greatly diminish the frequency and severity of the attacks although it may not (at first) prevent them altogether. It may be advisable to postpone the treatment until after an actual attack of lymphangitis has subsided, in case the patient should be unusually prone to allergic reactions at this time.

(iii) *The patient with hydrocele, elephantiasis, etc.* If he also has microfilariae or recurrent attacks of lymphangitis, then he ought to be given diethylcarbamazine. If he has neither, then it is doubtful whether administration of this drug is worth while, since it will probably have little effect upon the size of the lesions. On the other hand, even if it cannot be expected to do much good, it can do no harm, so there is no contraindication to its use. The proper treatment of gross elephantiasis of the scrotum is, of course, surgical and the results are usually satisfactory. The same is true of hydrocele. If surgical facilities are not available, considerable temporary relief for hydrocele may be obtained by tapping. Elephantiasis of the leg or arm is difficult to treat by surgical means and the results are seldom satisfactory unless elaborate plastic operations are done, and these are seldom possible in the circumstances. Much relief can be obtained, however, by palliative measures such as the application of an elastic bandage or similar means of support. The enlargement of the limb is due mainly to excessive fluid especially in the early stages. Removal of this by mechanical pressure reduces the size and weight of the limb and checks the further development of the deformity. It may be difficult, however, to persuade the patient to persevere. Diminution in the swelling of elephantiasis has been reported to follow the administration of cortisone (Markell and Kerrest, 1955), but this treatment does not seem suitable for general application.

(iv) *The patient with chyluria.* This is often very difficult to treat. It is worth while giving diethylcarbamazine, which will remove microfilariae from the blood and urine, but which will often fail to check the chyluria. This depends on obstruction to retroperitoneal lymphatics. Chief reliance should be placed on general measures such as rest, high protein diet, etc. The condition tends to stop (and to recur) spontaneously, and whatever treatment is in progress at the time will get the credit.

Mass Therapy

The most promising method of applying drugs for the control of filariasis is by mass therapy. Diethylcarbamazine would be given to all the carriers of microfilariae in the area and the treatment would be repeated at suitable intervals until practically all carriers were permanently cleared of infection. There would then be no source for new infections and the disease would be eradicated. This method is still at the pilot-trial stage but encouraging results have been reported from many quarters, and in Tahiti it has been applied to a large population with good effect. A detailed discussion cannot be given here. Briefly, the most effective and

also the best tolerated dose schedule seems to be an interrupted one, *e.g.*, 1 dose per month or 1 dose per week for 12 doses in the year. But in some areas, treatment once daily on 5 consecutive days may be more practical from the administrative aspect. In Tahiti the dose employed was 300 mgm. per adult once a month, but it is possible that a smaller dose might be sufficient. The programme requires repetition for several years. In the first year the whole population, or only the proved carriers, may be treated. In subsequent years, blood suveys should be made and only the carriers of microfilariae should be treated. The minor toxic effects which may be caused by diethylcarbamazine may render the mass therapy unpopular at first, but it has been found that this difficulty can usually be overcome by suitable education and propaganda. Administration of antihistamine drugs or calcium gluconate to prevent these minor disturbances has not been very effective and it is not worth while.

Loiasis

Treatment with diethylcarbamazine is usually very effective. For individual patients the dose schedule should be the same as that for bancroftian filariasis, *viz.*, 100 mgm. thrice daily for 21 days. If this is not completely successful in preventing all further symptoms it should be repeated one or more times, with an interval of one or two months between courses. During the treatment, thin white weals may appear under the skin; these indicate adult worms which have been killed by the drug.

Mass therapy for loiasis has been tried in one area with promising results.

Onchocerciasis

The therapy of onchocerciasis is much less satisfactory than that of wuchereriasis and loiasis, since the adult worms are not very sensitive to diethylcarbamazine. The most effective treatment is to give suramin intravenously, 1 gm. for an average adult, once weekly for 5 weeks; in heavily infected persons 10 weeks may be needed. This usually kills the adult worms and later the microfilariae disappear. After about the fifth dose there are often various reactions such as pains in the joints, etc., fever, and erythematous and pruritic eruptions. The fever may last a few days to 2 weeks. There may be transient conjunctivitis and photophobia. Suramin should be given only under medical supervision.

Diethylcarbamazine can be given for onchocerciasis. It removes microfilariae, but they soon return as the adult worms are not killed. It excites violent allergic reactions especially in patients with many microfilariae, the severity of the reaction being proportional to the density of the infection rather than to the dose. The skin of the infected parts (especially thighs, buttocks, lower abdomen and genitals) is hot, swollen and tender, and it itches severely for one or two days. There is pyrexia which may rise to 104°F. The corresponding lymph glands are swollen

and tender. The eyes (if infected) also show conjunctivitis and photophobia. These symptoms subside after 3–5 days and then large doses of diethylcarbamazine can be well tolerated.

In spite of these allergic reactions and of the fact that the microfilariae will return after a month or two, it is still worth while to give diethylcarbamazine for onchocerciasis. Relief from pruritus occurs promptly and may last for 18 months; and punctate keratitis rapidly clears up after treatment with diethylcarbamazine. When microfilariae are in the skin of the head, thus endangering the eyes, some treatment ought certainly to be given, either diethylcarbamazine or (less rapid in action) suramin. If the former, the dosage should be 25 mgm. on the first day, and 25 mgm. twice daily on the second day. Then if the reactions are not too severe, the full treatment of 100 mgm. three times a day for 10 days can be given. If the eyes are already infected, caution is necessary lest the reaction cause further ocular damage; the dosage on the first 4 days should be only half that just described. Patients treated for onchocerciasis with diethylcarbamazine should be kept under close supervision for the first 5 days, preferably in hospital, so that the effect upon the eyes can be observed and controlled. Diethylcarbamazine may also be usefully employed as a prelude to more radical treatment with suramin, or in certain persons, *e.g.*, Europeans, living in areas where they are much exposed to infected *Simulium* it may be usefully given every 6 months to keep down the infection.

Other Filarial Infections

For all practical purposes, the other forms of filariasis, *e.g.*, *D. perstans* and *Mansonella* infections, do not respond to diethylcarbamazine; and as these infections are non-pathogenic it is not worth while to attempt to treat them. Guineaworm is best treated by rest and gentle extraction of the worm by the standard methods. If the development of an infection could be diagnosed in advance (which is hardly ever the case) a course of diethylcarbamazine could be given.

References

(1) Hawking, F. (1955), The chemotherapy of filarial infections. *Pharmacological Reviews*, v. 7, 279. [*Trop. Dis. Bull.*, 1956, Aug.]

(2) Markell, E. K. & Kerrest, J. (1955), Treatment of elephantiasis with cortisone in French Oceania. A preliminary report. *Amer. J. Trop. Med. & Hyg.*, v. 4, 930. [*Trop. Dis. Bull.*, 1956, 470.]

SUMMARY OF RECENT ABSTRACTS *

VI. PLAGUE †

Epidemiology: Transmission

In 1919–29 plague constantly appeared in Istanbul and Antalya, Turkey, the infection apparently being introduced by ships; in 1947 an epidemic occurred far inland, near the Syrian border, which BERKE (p. 626) attributes to infection in wild rodents. The organisms in the seaport outbreaks were of *orientalis* type (see GIRARD, below), those of the inland outbreak of *mediaevalis* type. ÖZSAN and AKYAY (p. 446) describe this 1947 epidemic. The type of organism isolated belonged to the variety which is glycerol-positive and NO_2-negative (var. *mediaevalis*, see Girard, below).

A small outbreak of sylvatic plague is reported from Northern Rhodesia by WORSFOLD (p. 1081), who believes that the infection was introduced by multimammate mice.

MACCHIAVELLO (p. 359) has published a most useful series of papers on the reservoirs and vectors of plague, in which he gives lists of the fleas according to geographical distribution and spontaneous or experimental infection. The reservoir animals—naturally infected or experimentally susceptible—are listed geographically.

OLITZKI (p. 768) has found experimentally that the field mouse *Microtus guentheri* is relatively resistant to massive doses of *Pasteurella pestis*, which killed most of the white mice controls, and argues that though *M. guentheri* is common in the coastal plain of Israel, it was probably not the reservoir from which the plague of the Philistines originated in Biblical times, as has been suggested.

Plague has long been known to occur in wild rodents of the western States of the U.S.A., some near the Mexican border. VARELA and VÁZQUEZ (p. 972) now report finding *P. pestis* in prairie dogs (*Cynomys mexicanus*) in northern Mexico.

QUAN *et al.* (p. 534) have confirmed the classical finding of BACOT and MARTIN (1914) that fleas whose proventriculi have become blocked by masses of *P. pestis* are specially effective vectors of plague. They found that very much larger numbers of non-virulent than of virulent strains were needed to infect fleas. In some fleas the proventricular block was found as early as the second day but the rate of blocking did not reach 30–40 per cent. until 6–9 days after feeding. Virulence was not enhanced by passage through fleas. An apparatus for the experimental feeding of fleas, through membranes formed of the skins of small rodents, is described

---

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1955, v. 52. References to the abstracts are given under the names of the authors quoted and the pages on which the abstracts are printed.

† For previous articles on plague in this series see the July issues of the *Tropical Diseases Bulletin* each year since 1939.

by KARTMAN (p. 360), who notes that fleas feed as readily on preparations of human blood used for transfusion as on rat blood, but that they will not feed through Cellophane membranes.

A report on a large number of fleas collected from mammals and rodent nests in New Mexico is contributed by MORLAN (p. 972) who concludes that much more information on host-parasite relationships is needed before rodent-borne disease can be controlled economically.

In experiments on possible transmission of *P. pestis* by Triatominae AMES *et al.* (p. 152) found that the bugs can transmit the organism mechanically by contaminated mouth-parts shortly after the infecting feed, but not later. Mice which ingested infected bugs became infected, some developing pneumonic plague probably from aspiration of infected material into the lungs. The faeces of bugs which had recently fed on infected mice were infective to other mice only if inoculated immediately after the infecting meal.

Aetiology

The Yersin-Kitasato controversy is discussed by OGATA (p. 1081) who shows that his own father found that the Yersin organism was the true cause of plague, and the Kitasato organism a secondary invader. Ogata senior also suggested (in 1896) that plague was transmitted by the flea.

ENGLESBËRG *et al.* (p. 768) examined the oxidative metabolism of *P. pestis* grown under aerobic and anaerobic conditions, and the enzyme changes accompanying the shift from anaerobiosis to aerobiosis. These papers should be studied in full.

SANTER and AJL (p. 971) discuss the fermentation of glucose by *P. pestis*, and (p. 1191) its enzymes. THAL and CHEN (p. 629) have found that on media containing urea there was evidence of production of urease by *P. pseudotuberculosis*, but no such production by *P. pestis*; the former grows abundantly on desoxycholate citrate agar, but *P. pestis* grows only scantily.

GOODNER *et al.* (p. 628) found that the addition of bile salts to suspensions of *P. pestis* greatly increased the toxicity of the end product for mice. The lysis which occurs in suspensions was hastened in the first few minutes when bile salts were present, but the increased toxicity was only partly explained by this because the natural autolysate, when freed from cells, became much more toxic after the addition of sodium desoxycholate. This additional toxin is more labile than the ordinary lysate toxin; they may be immunologically distinct.

Experiments with *P. pseudotuberculosis* and the EV strain of *P. pestis* indicated that the toxin of the former is a true exotoxin, but that of the latter is not; SCHAR and THAL (p. 629) did not observe any cross immunity between the two toxins.

A method of classification of strains of *P. pestis* by means of the pattern of the zones of precipitation formed in a mixture of anti-plague serum and agar when a suspension of the organisms is floated on to it,

is described by RANSOM *et al.* (p. 627). By these means they found 3 different groups in 5 strains tested.

The double diffusion gel method was used by CHEN and MEYER (p. 1191) for the study of the diffusible antigens of *P. pestis* and *P. pseudotuberculosis* and their antibodies. Concentric rings of precipitation were observed in various zones where antigens and antibody met, and in this way rings corresponding to Fractions I and II and to 2 somatic antigens were recognized for *P. pestis*. With a non-virulent strain, and with *P. pseudotuberculosis*, only the 2 somatic rings were formed. The method is regarded as precise and useful for comparative studies.

DEVIGNAT (p. 40) discusses his classification of plague bacilli into the 3 varieties *antiqua*, *mediaevalis* and *orientalis*; the last 2 are probably mutation forms of the antique variety which may have had its home in the high plateaux of central Asia. There exist histories of 3 pandemics—the plague of Justinian (6th century) probably due to the antique variety, the Black Death (14th century) probably due to the mediaeval variety, and the pandemic of the early part of the present century, spread by sea all over the world, arising probably as a mutation from the antique variety. GIRARD (p. 41) recognizes 2 varieties, the first is glycerol-negative (var. *oceanica* or *orientalis*) and the second is glycerol-positive and does not produce nitrous acid (var. *continentalis*, which some observers regard as comprising var. *antiqua* and var. *mediaevalis*). Repeated transfer of *mediaevalis* through white rats did not alter its characters, and the author thinks that each variety remains true to type for indefinite periods, and that when two varieties are found simultaneously in the same region, as in Kenya, they have probably been introduced independently and at different times. He (p. 1082) makes the point that from the clinical point of view the 3 varieties of *P. pestis* are equal. He thinks that when infection in rats or wild rodents is found to be due to the *orientalis* variety it can be assumed that the original source of infection was the rat, whereas if one of the other two varieties is found it can be assumed that the source has been a recrudescence of an ancient focus of infection in the wild rodents of the locality.

JESIERSKI *et al* (p. 358) describe a strain of *P. pestis* var. *orientalis* recovered from the nasal mucus of a horse in the Belgian Congo. The strains corresponded in biochemical reactions to an avirulent strain used for immunization. The organism undoubtedly came from the horse, but it cannot be said with certainty that it was the cause of the disease (a swelling of the skull) from which the horse was suffering. The only previous reports of plague in large domestic animals relate to asses in Manchuria, and to a camel.

Pathology: Diagnosis

Chronic pneumonic plague was induced in monkeys by RANSOM and KRUEGER (p. 361) by a technique involving the inhalation of aerosol

suspensions of *P. pestis*. A description of the pathological findings is given; no evidence was seen of multiplication of the bacilli in liver or kidneys. In experimental pneumonic plague induced by intratracheal inoculation in monkeys, EHRENKRANZ and WHITE (p. 360) found that the liver was soon invaded by the organisms, with consequent functional disturbance which contributed to the fulminating course of the disease.

SILVERMAN (p. 42) describes the preparation of certain fractions from a saline extract of *P. pestis* which, when adsorbed by sheep erythrocytes, render these agglutinable by antiplague serum. This haemagglutination test was found to be more strictly specific and more sensitive in the diagnosis of plague than the bacterial agglutination tests now available. It can be used to measure the protection afforded by vaccination. NÉEL and GIRARD (p. 1192) claim that the haemagglutination test with erythrocytes treated with tannic acid is much more sensitive and specific than the classical methods of sero-diagnosis in plague. They discuss possible errors in technique in a paper which should be read in full.

HOYER and COURDURIER (p. 769) describe a precipitin test which is carried out by mixing suitable dilutions of anti-plague rabbit serum globulin with saline extracts of pooled suspensions of body tissues of persons dead of plague. The mixtures are incubated in capillary tubes. The precipitin titres ranged from 1 in 4 to 1 in 32 in a group of 4 cases, and in 2 out of 3 of them the tissue suspensions caused plague in guineapigs when applied to the excoriated skin.

WOODWARD (p. 1189) reports on plague in Madagascar where it was found almost impossible to study pneumonic plague because so few cases could be found. Plugs of tissue obtained by thrusting a large hollow needle into the lungs, liver and buboes of persons dead of plague were found to contain plague antigen, by precipitin tests with plague antisera. He gives an account of the control measures in use in Madagascar, including vacination, and of the extensive use of DDT for malaria control, which has been associated with a reduction in the flea population. Studies in the antibody patterns in Madagascar patients recovered from pneumonic plague as a result of treatment with antibiotics are reported by MCCRUMB *et al.* (p. 628). Various tests indicated the presence of antibodies during convalescence; antibodies against the envelope substance and against the toxins of *P. pestis* were found.

Control

A protective anti-rat measure advocated by HENTSCH (p. 1082) is to dig a trench 45 cm. deep and 40 cm. wide round each house in an infested village (in Java); rats in the infective stage are not able to cross such a trench if the walls are vertical, but the trenches require careful maintenance. The author shows that *P. pestis* can survive for at least 15 days in the bodies of infected fleas killed by DDT, so long as the fleas are not desiccated.

In an experiment on the control of flea vectors of plague on Californian ground squirrels by dusting their burrows with insecticides, Ryckman *et al.* (p. 153) found that one dusting with heptachlor, dieldrin or aldrin gave satisfactory control for 9 months, but that DDT was less effective.

Courdurier (p. 1190) shows that in 1954 only 17 cases of plague were diagnosed in Madagascar, and he gives an acount of the extensive programmes of vaccination with the live EV vaccine, which is still continued. No infection was found in 107,185 rats caught. Girard (p. 268) has shown that the EV vaccine gives protection to both mice and guineapigs not only against infection with virulent strains of the *antiqua* and *orientalis* varieties of *P. pestis* but also against a virulent strain of the *mediaevalis* variety. Even the most effective killed vaccines, such as the Haffkine vaccine, are said to be unable to protect guineapigs against virulent strains, though they do protect mice.

In a study of experimental immunization against plague Ehrenkranz and Meyer (p. 897), who used live EV vaccine, or a formalin-killed virulent strain of *P. pestis*, or capsular fraction I of virulent *P. pestis*, found that repeated vaccinations, spread over a long period, were much more effective than massive vaccinations given over a short period, and that to be effective the vaccine must provide Fraction I in adequate amounts. This may be already available, as in killed vaccines, but if live vaccines are used they must be able to produce it.

The administration of cortisone 4 hours before a dose of live avirulent EV 76 strain increased the fatality rate in mice, which is low with the EV vaccine alone, but Payne *et al.* (p. 898) found that this was not true with all avirulent strains, or with lysed toxins of *P. pestis*.

Chen and Meyer (p. 898) isolated a number of avirulent strains of *P. pestis* from old cultures by the "single colony picking" method. Some of them were highly protective to mice and others less so. Of 2 highly protective strains one was the most toxic and the other the least, so that there seems to be no relationship between toxicity and immunogenicity. Both strains contained high proportions of Fraction I.

Charles Wilcocks

MALARIA

In this section abstracts are arranged as far as possible in the following order:—Human malaria—*epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control;* Animal malaria—*monkeys, other animals, birds.*

Indian J. Malariology. 1955, Dec., v. 9, No. 4, 225–401, numerous illustrations. [Numerous refs.] **Silver Jubilee Number.**

This journal has undergone three changes of title: it started as the *Records of the Malaria Survey of India*, after 8 years it became the

Journal of the Malaria Institute of India, and in 1947 it took its last name, the *Indian Journal of Malariology*. The first editor was J. A. Sinton [whose recent death is widely regretted], the second G. Covell, and he was followed by the present editor, Jaswant Singh. The high standard of this publication has been maintained throughout the period; its contents have fallen into two main categories, surveys and control schemes of India and fundamental research on the parasite, vector, and anti-malarial drugs. Today, as with malaria institutes elsewhere, the activities of the institute itself have been widened to include other arthropod-borne diseases, and it is probable that its journal will have to follow suit. The Jubilee Number includes papers by past and present members of the staff and by foreign malariologists; these papers are reviewed briefly below.

J. A. Sinton (*Some lacunae in our knowledge of the malaria parasite*). This author was just the right person to enumerate and reflect on the problems still remaining in malariology; it is strange that after 75 years' work during which malaria has been more studied than any other protozoal diseases, serious gaps in our knowledge remain. Even the question of nomenclature is unsettled, because the discovery of the exoerythrocytic cycle suggests that the single genus *Plasmodium* is inadequate even for the human parasites, and probably *falciparum* should revert to the old genus *Laverania*. A coloured plate depicts parasites apparently outside the corpuscles and this question is discussed at length; it also shows the " vacuole " and the true nature of this object is stated to be still obscure, though it is probably part of a vesicular nucleus. The method by which the parasite undergoes schizogony is discussed. The cause of stippling of infected erythrocytes is still unknown; the changes are invisible *in vivo* and are probably mechanically produced. It has always been doubtful as to how many species or subspecies are responsible for malignant tertian malaria; various names have been employed such as *immaculatum*, *quotidianum*, *perniciosum*, *aethiopicum* but none has been fully accepted. The name *P. tenue* unfortunately is invalid for priority reasons; otherwise there would appear to be some justification for employing this designation for a parasite which possesses such a different morphology from that of the classical *P. falciparum*. An explanation for the failure of some species of *Anopheles* to become infected with malaria has never been given. Other unsolved problems are the existence of a malaria toxin, immunological tests and the nature of antibodies, and the origin of gametocytes.

R. D. Manwell (*Some evolutionary possibilities in the history of the malaria parasites*). This is an interesting paper which needs to be read in full; it cannot help being speculative in regard to the later stages, though it is clear that the malaria parasites must have arisen in the remote past from free-living ancestors. There are then two ideas of their descent, either from parasites of invertebrates or from Coccidia of vertebrates, and the author is inclined to the latter view. The most

ancient vertebrate hosts of *Plasmodium* and of *Haemoproteus* are reptiles; there is a striking resemblance between these parasites in reptiles and in birds which have a close evolutionary relationship. Malaria parasites are much less frequent in mammals, in which they have a spotty distribution; they perhaps represent here a "kind of after-thought", and their greater pathogenicity in this class of animals suggests that they are of more recent origin. It is interesting to note that birds and reptiles (accompanied probably by their parasites) go back before the tertiary period when blood-sucking Diptera had not yet arisen. Perhaps when more is known about the invertebrate cycle of *Plasmodium*, *Haemoproteus*, *Leucocytozoon* and *Hepatocystis*, a clearer picture will emerge of this evolutionary development.

P. C. C. Garnham and R. S. Bray (*Absence of cross-immunity between Plasmodium cynomolgi and Plasmodium gonderi*). *Plasmodium gonderi* and *P. cynomolgi* are the African and Asian representatives respectively of "benign tertian malaria" parasites in the lower monkeys. Their morphology is very similar, but the parasites differ in a number of minor points (as shown in a table) and in absence of cross-immunity. Monkeys immunized to *P. cynomolgi* were susceptible to *P. gonderi* and *vice versa*.

G. Macdonald (*A new approach to the epidemiology of malaria*). This paper gives a brief account of the author's views on the mathematical approach to the epidemiology of malaria, which have been explained in detail elsewhere [see this *Bulletin*, 1953, v. 50, 871]; here they are described particularly in relation to control of the disease in India. There are 4 principal factors concerned: the number of days gametocytes are patent, the number of vector mosquitoes which bite the carrier daily, the temperature (as influencing the rapidity of sporogony) and the mortality rate of mosquitoes (determining firstly the number of mosquitoes which survive to become infective and secondly the length of life of such infective mosquitoes, during which they continue to infect new people). With these factors, it is possible to work out the "reproductive rate", *i.e.*, the number of secondary cases which could potentially arise from the primary one—it may easily be 1,200. This basic calculation is profoundly affected by accessory factors such as degree of zoophily in the vector (*i.e.*, deviation from man to animals), degree of immunity in the host (whereby a corresponding number of infective bites are non-productive), superinfection of the mosquito. Two different types of malaria thus emerge—the stable or hyperendemic variety where the mosquito feeds chiefly on man and lives a long time, and the unstable or epidemic where the vector is less anthropophilic and is short-lived. In India much of the malaria belongs to the second category and further study of the factors involved might easily lead to elimination of the disease.

Jaswant Singh (*Some problems on chemotherapy of malaria*). The modern synthetic anti-malarial drugs provide an adequate treatment for

all acute attacks of malaria: drugs of the 4 aminoquinoline series clear the asexual parasites from the circulation, either by oral administration or in more severe cases by parenteral. Mepacrine and quinine have various defects, while proguanil and pyrimethamine are poor blood schizontocides, and sometimes give rise to resistance. Other stages of the life cycle are less easily eradicated, and the mechanism of action of the various drugs is little understood, though it is thought that all act by interfering with the metabolism of the parasite in its different phases. The metabolic processes of (1) the sporozoite, (2) the primary tissue forms, (3) the asexual erythrocytic stages, (4) the gametocytes and (5) the secondary tissue forms all probably differ, and even one species of parasite behaves differently from another. The main object today of chemotherapeutic research in malaria is to discover a drug which acts against all these forms, or at least against the blood and tissue schizonts.

J. M. Henderson (*Anopheles resistance in relation to malaria control programme planning*). After ten years' application of the residual chlorinated insecticides throughout the world, it is astonishing how little resistance has arisen in the vector anopheline mosquitoes, only 4 out of about 50 species having shown any signs of this process (*viz.*, *Anopheles sundaicus* in Indonesia, *A. maculipennis*, *A. sacharovi* and *A. superpictus* in Greece or the Lebanon) [see Pampana, p. 843]. It remains a threat, however, and it is suggested that research should be directed (a) to develop even more effective insecticides, (b) to find insecticides with differing periods of action and (c) to discover new techniques of application.

B. N. Mohan (*Sporogony cycle of malaria parasites in resistant and non-resistant strains of mosquitoes after exposure to DDT*). The results of the experiments described in this interesting paper indicate clearly that (1) mosquitoes which have developed a resistance to the synthetic insecticides remain good vectors of malarial parasites and (2) the insecticide itself has no effect on sporogony of the parasite. These observations were made on the 43rd and 44th generations of DDT-resistant *Culex fatigans* infected with *Plasmodium relictum*, and included experiments in which the mosquitoes after infection were exposed to the insecticide. A control series with susceptible mosquitoes showed similar infection rates, and in both groups exposure to DDT failed to influence the course of sporogony. Next, similar experiments were carried out with resistant (to a much less degree) and non-resistant strains of *Anopheles fluviatilis* and *Plasmodium vivax* and *P. falciparum*, and again both showed an equal degree of susceptibility. Finally a non-resistant strain of *Aëdes aegypti* was allowed to feed on chicks infected with *P. gallinaceum* and was exposed before or after feeding to DDT. Few survived but the incidence of infection in the survivors was about the same as in a control group. DDT had no effect on the viability of these sporozoites or on the development of the parasite in the bird if given orally to the latter.

D. K. Viswanathan, T. R. Rao and A. V. Halgeri (*Observations on*

some aspects of the nocturnal behaviour of Anopheles culicifacies). *Anopheles culicifacies* is the most important vector of malaria in India and this paper describes studies near Poona on the behaviour of the adult at night; huts with window traps and baited with buffaloes were used. Ninety per cent. entered the hut before midnight, and about one-third left during the course of the night. Most of the feeding took place before midnight, and multiple feeding was probably common. The treatment of a hut with DDT offered no bar to entry or feeding.

S. R. Christophers (*Policy in relation to malaria control*). The policy of malaria control must take into account what is desirable, what is possible, and the method of application; it must be accompanied by (a) its actual object and (b) plans to see how the object has been achieved. Two things have revolutionized control in recent years: the discovery of effective anti-malarial drugs and of the residual insecticides. The application of control is considered in particular regard to India, and it is emphasized that both for investigation and for the carrying out of control schemes some permanent organization is necessary and India is fortunate in possessing an Institute which leads the world in this regard. Similar organizations elsewhere are highly desirable; an institute has been recently established in East Africa under the directorship of Dr. D. Bagster Wilson.

G. Covell (*Developments in malaria control methods during the past forty years*). Knipe, Pampana and Pal in other papers describe in some detail the new approach which Christophers has summarized. G. Covell takes it from the historical standpoint and shows how methods of control have developed in the last 40 years, from the original attack on the anopheline larva to the killing of adults first with pyrethrum and now with DDT and the synthetic insecticides. E. J. Pampana (*Some malaria eradication problems as visualized in 1955*) emphasizes the desirability of eradication as the aim, even though it may not always be feasible. Today eradication is more than ever important because signs of resistance to DDT in certain vector species (*Anopheles sacharovi*, *A. superpictus*, *A. sundaicus* and *A. stephensi*) are being observed. If eradication of malaria is limited in extent, then it is essential that "epidemiological surveillance" be introduced to ensure that immigrant carriers are sterilized of their infections. The infant parasite rate is the index to watch, and usually 2 years of insecticidal treatment are necessary to reduce it to zero. Correct timing of the programme is an essential of success [as it is for all "eradication" as opposed to "control" schemes]. Rajindar Pal and M. I. D. Sharma (*Malaria control by the use of insecticides*) give a useful list of 60 malaria vectors of the world in relation (a) to their biting and resting habits and (b) to their susceptibility to the modern insecticides; information is deficient in respect of at least 25 of these species. F. W. Knipe (*The changing aspect of hand-operated equipment in malaria control*) discusses the all important question of equipment, the *sine qua non* of malaria control. Fifty years ago it was primitive

and was mainly apparatus for spreading oil, today the question is that of applying residual insecticides in houses. The final result is the development of two types of hand operated sprayers—the hand-compression and the stirrup-pump. The latest features include a stainless steel tank, welded seams to prevent leakage, Shrader valve for pre-pressurizing, plastic leak-proofing and a quickly detachable bayonet connexion for the discharge pipe. The author states that models are now so perfected that a malaria officer knows that he has dependable equipment, but concludes that although it is far superior to yesterday's, there is still room for improvement.

B. A. Rao (*The national malaria control programme of India*), D. R. Mehta (*Malaria control in the Punjab (India) with special reference to the national malaria control programme*), and V. V. Rao (*On the possibility of A. sundaicus eradication in India*) discuss some of the problems of malaria control in India, where at present a Five Year Plan is now (1955) in its third year. B. A. Rao describes this plan, probably the biggest in the world today: it is to protect the 200 million people at risk from the disease which was responsible for nearly a 100 million cases and nearly a million deaths a year. Today 162 million people are already living under the DDT umbrella (100 mgm. per sq. foot applied twice), and interim results are given in 3 appendices. The results are analysed in more detail for the Punjab State by D. R. Mehta, who emphasizes the need of " strategic control " once transmission has been stopped, so that malaria will not reappear. V. V. Rao in an interesting paper traces the spread of *A. sundaicus* in India, particularly in the coastal area of Lower Bengal, Chilka Lake area (Orissa) and further South to near Vizagapatam. This species is one which elsewhere has developed a resistance to DDT so the author considers that antilarval measures by a variety of methods should be the primary means of attack, though combined with indoor spraying. *P. C. C. Garnham*

Trinidad Govt. **Annual Report of the Malaria Division, Health Dept., Trinidad & Tobago. 1954.** 65 mimeographed pp., 6 graphs (4 coloured) & 1 pl.

The report records in full detail and illustrates with graphs and numerous lengthy tables all the activities of the Division. They include the examination of blood films, larval and adult mosquito studies, malaria control by larvicidal and imagicidal means, the management of the malaria eradication programme in Tobago, and in this particular year the control of *Aëdes aegypti* owing to the occurrence of yellow fever in the island. Among much which is of local concern there are several items of more general interest. Miss Wall records an unsuccessful effort to establish *Anopheles aquasalis* in colony, failure being due to inability to bring sufficient numbers through the larval stage, which may be due either to the exposure of the insectary to insecticides or to the characteristics

of the cages and breeding places. An account is given of the control of bromeliad malaria and of the rate of re-infestation of trees with bromeliads after their destruction by copper-sulphate. Many techniques were used for malaria control but the arrival of yellow fever made it possible to treat all houses in Port of Spain and a large proportion elsewhere with DDT. The malaria eradication project in Tobago, which had been carried out in conjunction with the Rockefeller Foundation and has now been passed over to the Government of Trinidad, appears to have been successful and of 2,507 slides examined all were negative.

In the course of anti-*Aëdes* measures by the application of DDT 1 part per million to breeding places, it was realized that the dose was ineffective and subsequent laboratory trials showed that 1 p.p.m. killed only 2·8 per cent. of larvae after 24 hours and 20 p.p.m. no more than 46·4 per cent. This work continues; it undoubtedly shows a resistance to DDT by *Aëdes aegypti* in Trinidad, which may have been acquired in the course of 8 residual treatments of the area from which specimens were collected.

G. Macdonald

Colbourne, M. J. & Edington, G. M. **Sickling and Malaria in the Gold Coast.** *Brit. Med. J.* 1956, Apr. 7, 784–6. [17 refs.]

The authors have studied two populations in the Gold Coast, Frafras in the Northern territories and inhabitants of Accra (mainly Ga) in the south. In 46 babies examined in Accra over a period of 6 months it was found that at the end of that time more than half of them had suffered from malaria—6 of 11 sicklers and 22 of 35 non-sicklers. The parasite densities were greater in the non-sicklers but the authors do not want too much emphasis to be placed on this finding. The numbers observed were small; and one non-sickler had a density of well over 50,000 parasites per cmm. With small numbers this one heavy infection weighted the figures in favour of the sicklers. The two surveys in Accra and in the Northern Gold Coast show very different results. In Accra there was a lower parasite rate in sicklers at all ages, 1,015 being examined. In the Northern Gold Coast there was a difference only in the infants, but the sample included only 7 sickling infants. The density of the parasites followed the pattern of the parasite rates: a significant difference in favour of the sicklers was seen in Accra and almost none in the Northern Gold Coast. Two explanations for this difference are put forward by the authors; one that the transmission of malaria is more intense in the Northern Gold Coast than in Accra and hence in the Northern Gold Coast it would be necessary to examine very large numbers of children under the age of 1 year to discover whether sickling has any protective action; and another that no account was taken in this investigation of the presence of haemoglobin C in these populations. If haemoglobin C had a similar protective function to that of haemoglobin S a mere comparison of sicklers and non-sicklers would take no account of additional

influences which would obscure the relationship between malaria and sickling.

An additional interesting observation was made on 68 schoolchildren in Accra, of whom 14 sickled. For one year they were kept free from malarial parasites by suppressive drugs. During the subsequent year suppressive drugs were withdrawn; 7 of the 14 sicklers and 19 of the 54 non-sicklers became infected during this year. The average density of infection in the sicklers was twice as high as that in the non-sicklers. These results suggest that in this age-group sickling provides little protection against the milder clinical effects of this disease.

The sickle-cell tract was not found to give protection against *P. malariae* infection, and this is discussed. [See also this *Bulletin*, 1946, v. 43, 774; 1947, v. 44, 1091; 1954, v. 51, 720.] *H. Lehmann*

See also p. 921, Bezon, A propos d'une éventuelle résistance des sicklémiques à l'endémie palustre à *Pl. falciparum*. [**The Possible Resistance to Endemic** *P. falciparum* **Malaria in Sicklers**]

O'Rourke, F. J. **Korean Malaria in Canada.** *Canadian J. Pub. Health.* 1955, Oct., v. 46, No. 10, 400–406, 1 chart. [18 refs.]

There have been 21 cases of malaria among 327 veterans returned from Korea to south-western Ontario, and 152 among 1,350 returned to the Montreal area [this *Bulletin*, 1953, v. 50, 474, 906]. A reservoir from which a spread could occur is therefore being created. There are 6 indigenous species of anopheline, *A. quadrimaculatus*, *A. freeborni*, *A. walkeri*, *A. punctipennis*, *A. occidentalis* and *A. earlei*, of which the first two are known as carriers in the U.S.A., while *A. walkeri* has also been found infected. There are no Canadian data on their capacity as carriers or on their feeding habits. The temperature exceeds the minimum needed for the development of plasmodia for a part of the year over much of southern Canada, and a review of these conditions shows that there is a possibility of small outbreaks of malaria occurring, although the danger is not large and could be reduced by treating all soldiers returning from malarial areas with primaquine in doses of 15 mgm. of the base per day for 14 consecutive days. *G. Macdonald*

Languillon, J., Mouchet, J. & Rivola, E. Contribution à l'étude du *Plasmodium ovale* (Stephens 1922) dans les territoires français d'Afrique. Sa relative fréquence au Cameroun. [**Contribution to the Study of** *Plasmodium ovale* **(Stephens 1922) in the French African Territories; Its Relative Frequency in the Cameroons**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 6, 819–23, 1 map.

Malaria surveys on children between the ages of 1 and 9 years were carried out from June to September 1955 in the " forest zone " and the

"western mountains" in the Southern Cameroons. In the former *Plasmodium ovale* was detected 19 times, giving a rate of 0·54 per cent. among 3,483 children; in the latter 6 times, giving a rate of 0·42 per cent. among 1,400 children. The infections were mixed with either *P. falciparum* or *P. malariae*, or both, in all but 4 patients. The morphology of the parasite was typical of the species: mature schizonts contained 8 merozoites; most of the infected corpuscles showed the characteristic distortion; gametocytes were present in half the infections. The anopheline population in the huts comprised *Anopheles gambiae*, *A. moucheti*, *A. funestus*, *A. nili* and *A. marshalli*. *P. C. C. Garnham*

Covell, G. **Quartan Stippling.** *J. Trop. Med. & Hyg.* 1956, Feb., v. 59, No. 2, 28–30.

The author discusses the origin and appropriateness of the term "Ziemann's stippling", which is commonly used to describe the dots revealed in erythrocytes harbouring *Plasmodium malariae*. From a perusal of the literature, relevant quotations from which are given and critically assessed, he concludes that "It is impossible to say with certainty who first described the characteristic stippling seen in red blood cells invaded by quartan malaria parasites". On this account he proposes that this character should not be associated with any personal name, but should be designated merely as "quartan stippling".

C. A. Hoare

Shute, P. G. & Maryon, M. **Transmission of *Plasmodium malariae* by Laboratory-Bred *Anopheles maculipennis* var. *atroparvus* Meigen.** *Ann. Trop. Med. & Parasit.* 1955, Dec., v. 49, No. 4, 451–4.

Plasmodium malariae is notoriously difficult to transmit by mosquitoes. Between 1928 and 1945, 19 batches of *Anopheles maculipennis* var. *atroparvus* were fed at Horton Malaria Reference Laboratory on patients whose blood showed male and female gametocytes; 6 batches became infected with scanty oöcysts in the midguts, but no sporozoites appeared in the salivary glands. Another attempt was made in 1954, with a Lagos strain of the parasite, when the mosquitoes were fed once on a patient on the 6th day of fever (10th day of parasitaemia), male gametocytes being present in very small numbers (less than 5 per cmm.) in the blood. Seventy-two midguts were dissected and oöcysts (never more than 4) were found on 5; 45 glands were examined and sporozoites were found in 8. The oöcysts showed the characteristic distribution of pigment in a peripheral cluster, and when a new patient was bitten by the infected mosquitoes, a typical quartan fever arose 37 days later. The visible parasite incubation period was 35 days (or 12 days less).

Two cases of persistent quartan malaria are described; in one the infection had lasted 32 years, in the other 12 [this *Bulletin*, 1944, v. 41, 1002; and Lentini and Tecce, below, p. 851]. *P. C. C. Garnham*

Mariani, M. & Cefalù, M. Specie anofeliniche di Sicilia. Aggiornamento al 1955. [**Anopheline Species in Sicily. Position in 1955**] *Riv. di Malariologia.* 1955, Dec., v. 34, Nos. 4/6, 231–9, 3 figs. & 1 graph. [20 refs.] English summary (7 lines).

The authors describe the habitats of the adults and larvae of the anopheline mosquitoes of Sicily.

Previously known in the island were the species *Anopheles claviger*, *A. m. labranchiae* and *A. superpictus*; to these, 3 more are now added, ***A. algeriensis*** recorded in 1954, *A. hispaniola* and *A. marteri* recorded in 1955. The nomenclature used in this paper is that of Buonomini and Mariani 1953. [See this *Bulletin*, 1954, v. 51, 668]. *H. S. Leeson*

Loddo, B. Focolai larvali di *Anopheles labranchiae* e di *Anopheles sacharovi*. [**Larval Breeding Places of** *Anopheles m. labranchiae* **and** *A. sacharovi*] *Riv. di Malariologia.* 1955, Dec., v. 34, Nos. 4/6, 267–72. English summary (3 lines).

Senevet, G. & Andarelli, L. Les Anophèles de l'Afrique du Nord et du bassin méditerranéen. [**The Anophelines of North Africa and the Mediterranean Basin**] With a preface by Edmond Sergent. 280 pp., 66 figs. [1956.] Paris (VI^{e}): Editions P. Lechevalier, 12 Rue de Tournon. [3,000 fr.]

This work on the anopheline mosquitoes of all the lands surrounding the Mediterranean Sea is in 3 parts. The first contains an account of the morphology of the genus *Anopheles* describing in particular those characters of importance in the identification of species and giving some instruction on the preparation of material for examination.

The main part is the second which occupies some 170 pages and contains full descriptions of 17 species and their varieties. These descriptions are illustrated by 66 figures and 6 plates showing important anatomical details. Included in this part are brief notes on geographical distribution, altitudes, seasons, breeding places, other biological data and on the relation to malaria transmission of the various species. *Anopheles gambiae* is included in this part because there are one or two doubtful records of its occurrence at points in North Africa. *A. turkhudi* is very briefly mentioned by those characters which separate it from *A. hispaniola*.

In the third part are details of the geographical distribution of these anophelines with some references to localities and authors. There is also a general key to the identification of all stages of all the species, a separate key to those occurring in France and another to the species of the Western Mediterranean region. There is no separate key to species of the Eastern Mediterranean countries; readers interested in this region should therefore use the general key.

Important vectors of malaria in parts of the region are named as *Anopheles m. labranchiae*, *A. m. atroparvus*, *A. sacharovi*, *A. superpictus*. Species which could be vectors locally are given as *A. claviger*, *A. m. subalpinus*, *A. sergenti*, *A. d'thali*, *A. multicolor*, *A. pharoensis*. Anophelines quoted as of doubtful, limited or no importance are *A. marteri*, *A. plumbeus*, *A. m. maculipennis*, *A. m. messeae*, *A. m. melanoon*, *A. coustani*, *A. hyrcanus pseudopictus*, *A. hispaniola*. There is no evidence regarding *A. broussesi*.

This is a reference book which will be used by malariologists and entomologists seeking information first about the identity of anophelines in the Mediterranean countries and secondly about their biology. It is also a guide to the relevant literature, for the bibliography runs to over 350 entries. *H. S. Leeson*

Ovazza, M. & Neri, P. Vecteurs de paludisme en altitude (région d'Addis Abeba, Éthiopie). [**Vectors of Malaria at High Altitudes in the Addis Ababa Region, Ethiopia**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 5, 679–86, 1 fig.

The authors give an account of their investigations into the anopheline fauna of the country around Addis Ababa, Ethiopia, to explain the occurrence of cases of malaria in the city.

The survey was done in 1953–55 and the area studied extended from Addis Ababa in the north, south-eastwards to Bichouftou, 48 km. (30 miles), and south to the power station, some 70 km. (45 miles) away.

Addis Ababa is situated in mountainous country at altitudes between 2,470 and 2,580 metres (approximately 8,100–8,500 feet). South and south-eastwards the altitude falls until at Bichouftou and the power station it is about 1,950 metres (approximately 6,400 feet).

In the city the two anophelines most frequently encountered were *Anopheles christyi* and *A. cinereus*, neither of which seriously attacks man. Two other species found were *A. demeilloni* and *A. garnhami*. Larvae of *A. macmahoni* and *A. coustani ziemanni* were also recorded. The breeding places of *A. gambiae* were not found though two females were captured near the railway station in the lower part of the town near Filoha at 2,470 metres (8,100 feet). It is in this part of the town that cases of malaria sometimes occur. Numerous cases of malaria occur annually in the villages around the artificial lakes and in the vicinity of the power house (1950 m. = 6,400 ft.) and at Akaki, 23 km. (15 miles) south east of Addis Ababa at 1,950–2,100 m. (6,400–6,900 ft.).

Larval collections in these localities contained larvae of *A. gambiae*, *A. christyi*, *A. coustani*, *A. demeilloni*, *A. garnhami*, *A. cinereus* and *A. squamosus*. Adults were taken of all these except the last 2 and adults of the first 3 occurred in houses.

The present survey was done through 2 abnormally dry rainy seasons

but as the combination of favourable conditions provided in the Akaki valley by the presence of the warm springs, the artificial lakes and the sheltered gorges, encourages the survival of *A. gambiae*, it seems not unlikely that this mosquito could in certain circumstances extend its upward range and reach suitable breeding places in the warm springs of the Filoha quarter of Addis Ababa although they are another 400 m. (1,300 ft.) higher and above the previously suggested limit of 2,000 m. (6,500 ft.). [See also this *Bulletin*, 1943, v. 40, 744.] *H. S. Leeson*

Lips, M. & Hamon, J. Contribution à l'étude des Culicidés (Diptères) de la région Éthiopienne. Description de la larve, de la nymphe et du mâle d'*Anopheles austeni* Theobald 1905. [**Observations on Mosquitoes of the Ethiopian Region. Larva, Nymph and Male of** *Anopheles austeni*] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 6, 872–82, 6 pls.

Ansari, M. A. R. & Nasir, A. S. **The Value of Maxillary Index in the Identification of Mosquito Races.** *Pakistan J. of Health.* 1955, Apr., v. 5, No. 1, 37–43, 3 figs. [16 refs.]

A study of the maxillary index of a random sample of 200 *Anopheles culicifacies* from villages around Lahore showed the mean figure of 12·32 which brings the species within the paucidentate and anthropophilic group [this *Bulletin*, 1955, v. 52, 120]. The authors considered also thickness and length of the maxillae and tabulate the data obtained.

H. S. Leeson

Gabaldon, A. & Cova-Garcia, P. Zoogeografía de los anofelinos en Venezuela. IV Su posición en la región Neotrópica y observaciones sobre las especies de esta región. [**Geographical Distribution of Anophelines in Venezuela. IV The Position in the Neotropical Region and Observations on the Species found there**] *Rev. Sanidad y Asistencia Social.* Caracas. 1952, May–Aug., v. 17, Nos. 3/4, 173–210, 12 figs. on 12 folding pls. [23 refs.]

Schneider, J. & Hartmann, L. Paludisme et réaction de Henry. La réaction de Henry dans le diagnostic du paludisme. [**Henry's Reaction in the Diagnosis of Malaria**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 4, 552–64.

The authors have re-examined a flocculation test devised by Henry (*Constantine Médical*, 1953, v. 4, 1) which was devised to act as a diagnostic test for malaria. It was found that this test was non-specific,

and in liver disease in non-malarial persons went closely parallel with other serum protein lability tests, notably with McLagan's thymol turbidity test. Its results are not related to the malarial infection but to the resulting haemolysis; thus the reaction can be negative when malarial infection can be shown to exist by examination of the peripheral blood.

H. Lehmann

Lentini, D. & Tecce, T. Recidiva a lunga scadenza di infezione malarica quartana. [**A Very Late Relapse of Quartan Malaria**] *Riv. di Malariologia*. 1955, Dec., v. 34, Nos. 4/6, 259–65, 1 chart. [28 refs.] English summary (3 lines).

The authors report on a case in which a relapse of quartan malaria occurred after at least 45 years of freedom from signs and symptoms of the disease. The subject was a 70-year-old nun, who had entered a " closed " religious order at the age of 24, and who had never since left her convent, which is situated in the central part of Rome, so that any chance of indigenous infection can be excluded. She had a past history of various febrile illnesses before entering the convent and had lived in parts of the Roman Campagna where malaria was prevalent and where she had taken prophylactic quinine from time to time, the drug being distributed free to the inhabitants by the local authorities.

She was admitted to hospital from her convent after about 2½ months of febrile attacks, with rigor and sweating, each lasting about 12 hours and at first recurring at about weekly intervals; after some 40 days a quartan periodicity became established. There was considerable spleen enlargement and, after many specimens of peripheral blood had proved negative, the malaria parasite was demonstrated in films of medullary blood obtained by sternal puncture. The results of liver puncture were negative.

Following the sixth attack after admission to hospital the patient has been given 1·50 gm. of quinine sulphate daily, starting 40 hours after the latest attack. There has since been only one more attack, and this was of short duration and it was possible to discontinue quinine treatment after 5 days. There has been a progressive reduction of the spleen to about one-quarter of its size on admission, and the patient was discharged, much improved in health, after an apyrexial period of 30 days.

As a theory to suggest the mechanism of such relapses in malaria, the authors suggest that the antibodies which the host may have developed as a result of previous infection cannot reach such schizonts as are within the liver cells, though they destroy such merozoites as find their way into the blood-stream before these can attack the red blood cells. Some merozoites survive by finding their way back into liver cells.

J. Cauchi

DE PAOLA, Giovanna. Osservazione di un caso di malaria da trasfusione con complicanza renale. [**A Case of Transfusion Malaria with Renal Complications**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1956, Jan., v. 37, No. 1, 15–16.

A man of 52, who had suffered from nephritis in childhood, developed melaena in September 1953, as a result of a duodenal ulcer of 4 years' standing. On the 24th of that month he received a transfusion of 250 cc. of blood. On 19th October he developed fever and chills. No malaria parasites were found at that stage. Treatment with antibiotics was ineffective. The patient now had oliguria, albuminuria, haematuria, casts in the urine, oedema and hypertension. On 2nd November a careful blood examination revealed the presence of trophozoites and schizonts of *Plasmodium malariae*. After the intramuscular injection of 2 gm. of quinine daily for 2 days, the fever did not reappear. The treatment was completed with mepacrine. Within 10 days, the renal manifestations had almost entirely cleared and the patient recovered gradually. He had never suffered from malaria or lived in an endemic area.

The renal syndrome was presumably related to the patient's previous history and was stimulated by the malaria: nevertheless the anti-malarial treatment cured it almost completely.

H. J. O'D. Burke-Gaffney

BEAUZAMY, I., HASSEN, I. & LE MAPPIAN. Un cas de paludisme après traitement préventif régulièrement suivi. [**A Case of Malaria following Regular Suppressive Treatment**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 6, 817–19.

NIETO CAICEDO, M. Experiencias Venezolanas con las drogas anti-malaricas de la serie 4-aminoquinolinas. [**Venezuelan Experience with Anti-Malarial Drugs of the 4-Aminoquinoline Series**] *Rev. Sanidad y Asistencia Social.* Caracas. 1951, May–Aug., v. 16, Nos. 3/4, 317–441. [Numerous refs.]

PAULINI, E. Método espectrofotométrico para a dosagem da Cloroquina. [**Spectrophotometric Method for the Estimation of Chloroquine**] *Rev. Brasilcira Malariologia.* Rio de Janeiro. 1955, July, v. 7, No. 3, 329–32, 1 fig.

The English summary appended to the paper is as follows:—

"The author investigated the ultraviolet absorption of chloroquine in destilled water. The maximum absorption was observed at 360 milimicra. The Lambert-Beer's law is valid for the concentration range of 0,000–0,02 g/l. The spectrophotometric method offers a simple, specific, and rapid means for the determination of this antimalaric drug in a

variety of products, such as tablets, or chloroquinized table salt. The accuracy of the determination is ±1%."

Pinotti, M., Soares, R., Monte, R., Paulini, E. & Vinha, C. Experiências com o sal cloroquinado em doentes hospitalizados. [**Experimental Treatment of Patients in Hospital with Chloroquine Common Salt Mixture**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, Jan., v. 7, No. 1, 25–36. English summary.

For two and a half years the authors have continued experiments designed to determine the efficacy of the treatment of malaria, in patients in hospital in the Federal District, with chloroquine mixed with table salt. The daily doses of chloroquine administered varied from 0·045 to 0·010 gm. base. All the doses used were sufficient to control the fever and eliminate blood parasites in patients inoculated either with *P. malariae* or *P. vivax*. All patients were permanently free from infection within periods of 1 to 3 months of treatment except those treated with daily doses of 0·010 gm. base. A daily dose of 0·030 gm. base is sufficient and is recommended. No signs of toxicity appeared in patients who continued the treatment for 2 years. *Norman White*

Pinotti, M., Lôbo, A. G. S., Damasceno, G. & Soares, R. Experiências de campo com o sal cloroquinado. [**Field Experiments with Common Salt and Chloroquine Mixture**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, Jan., v. 7, No. 1, 5–23. English summary.

Pinotti has previously described a method of combating malaria by the addition of chloroquine to the table salt used daily by the population in the preparation of food [this *Bulletin*, 1955, v. 52, 10]. The method was specially applicable to those outlying parts of Brazil where the population lives in primitive shelters quite unsuitable for residual DDT spraying, or where the population is so sparse and scattered in country lacking easy means of communication as to make spraying operations impracticable or prohibitively costly. Thirdly, there are parts of Brazil, chiefly in the central plateau, where the vector, *Anopheles darlingi*, attacks man in the open air.

The present paper describes the results obtained by this method of control in three areas of Brazil, a central area in the state of Pará where *A. darlingi* is the vector, a coastal area in the state of Maranhão where the vector is *A. tarsimaculatus*, and in islands off the coast of the state of Paraná where the vector is *A.* (*Kerteszia*) *bellator*.

In places in Pará where the daily dose was 0·045 gm. base, the parasite rate fell to zero by the end of the fifth month of treatment; the parasite rates in control places remained unchanged. Equally good results were obtained in other places with a daily dose of 0·030 gm. base.

The results obtained in the states of Maranhão and Paraná were similar. The authors conclude that the method is of great value and should make an important contribution towards the eradication of malaria in the Amazon basin. *Norman White*

Arnold, J., Alving, A. S., Hockwald, R. S., Clayman, C. B., Dern, R. J., Beutler, E., Flanagan, C. L. & Jeffery, G. M. **The Anti-Malarial Action of Primaquine against the Blood and Tissue Stages of *falciparum* Malaria (Panama, P-F-6 Strain).** *J. Lab. & Clin. Med.* 1955, Sept., v. 46, No. 3, 391–7, 4 figs.

The subjects of this experiment were non-immune white volunteers, inmates of Stateville Penitentiary, Illinois.

Five volunteers were inoculated by mosquito bite with a strain of *Plasmodium falciparum* originally isolated from a resident of El Limon, Panama, and known as P-F-6. Each volunteer was given one dose of 30 mgm. primaquine on the day before inoculation, on the day of inoculation and on each of the 6 following days. None developed malaria. A group of 9 men was also completely protected by 30 mgm. primaquine given twice weekly for 4 weeks. Primaquine evidently has a powerful effect on the early tissue stages of the parasite, which probably undergo radical metabolic changes which would tend to cause a variation in response to the drug on different days during the pre-patent period.

It was necessary first to establish the period during which only tissue forms exist in the body. Ten men were inoculated with sporozoites, and 100 to 500 cc. of blood were withdrawn from 5 of them on day 5 (120 hours after inoculation) and from the other 5 on day 6 (144 hours after inoculation) for injection into fresh volunteers. In no case did the recipients develop malaria. It was therefore concluded that under the conditions of these experiments metamorphosis of parasites in the tissues is not completed until after day 6 (144 hours after inoculation).

To determine the pattern of drug action in the incubation period 95 volunteers were inoculated by mosquito bite as before and were then given a single test dose of primaquine (either 10, 15, 30 or 45 mgm.) on the first, third or fifth days after inoculation. The dosage-response curve suggests that the tissue forms undergo a marked change in their response to primaquine, reaching maximum susceptibility on the third day and finally developing a highly resistant stage similar to that found in circulating trophozoites. It is suggested that the parasite changes biochemically, so that by the fifth day it is nearly independent of the metabolic pathways reached and inhibited by therapeutic doses of the drug.

To test the effect of primaquine on the circulating blood forms of *P. falciparum* malaria, a group of 6 men were inoculated as before and were left untreated till blood forms were demonstrated on 2 successive days in

thick blood smears. Four of them were then given 30 mgm. primaquine daily. In 3 cases the patients became too ill to justify continuation of the experiment and their infection was accordingly terminated with chloroquine; the other responded well. The remaining 2 men were treated with 45 mgm. primaquine, but in neither case was the response satisfactory and the infection had to be terminated with chloroquine.

The authors conclude that primaquine should never be relied on to control parasitaemia in non-immune subjects without concurrent suppressive therapy. *G. Covell*

Zach, J. Zur Wirkung des 2,4-diamino-5-P-chlorophenyl-6-äthyl-pyrimidins (Daraprim) auf das hämatopoetische System. [**The Effect of Pyrimethamine on the Haematopoietic System**] *Klin. Woch.* 1956, Feb. 1, v. 34, Nos. 5/6, 137–9. [12 refs.]

Fifteen rats, weighing 200–250 gm., were given 25 mgm. Daraprim (pyrimethamine) intraperitoneally, and then 25 mgm. subcutaneously each day until death. Daily counts were made on the blood cells, and immediately after death smears were made from the bone-marrow. After 2 days, 11 rats survived; after 4 days 6; and after 5 days only 1 rat. The erythrocyte count diminished rapidly in almost a linear fashion, beginning with a fall of 1·5 million in the first 24 hours and 0·65 million a day thereafter. The reticulocyte value, which was originally 22–44 per 1,000, showed a diminution to 4·5 per 1,000. The haemoglobin fell to 50 per cent. at death. The colour index, which was initially 0·6, rose in 12 of the animals to 0·7–0·8.

The leucocyte count also diminished in linear fashion. The granulocytes dwindled to a complete granulocytopenia, while the lymphocyte count remained approximately constant. The lymphocytes showed nuclear pyknosis with multiple large dark staining inclusions in the nucleus. The thrombocytes diminished by about one-third, but there were no haemorrhagic symptoms. The bone-marrow showed extreme depression of erythropoiesis, and also of granulopoiesis. The reticulum cells, plasma cells and macrophages were increased in number, but they showed degenerative changes. Megakaryocytes were usually found in the smears only as involution forms.

It is concluded that these toxic doses of Daraprim cause both a depression of haematopoiesis and a direct haemolysis. *F. Hawking*

Kraan, H. **Malaria Control in North-Holland during and after the 1946–1948 Epidemic.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1955, Dec., v. 7, No. 4, 347–58, 2 graphs & 1 map. [10 refs.]

Malaria control in Holland is based on the epidemiological studies and recommendations of Swellengrebel and de Buck [this *Bulletin*, 1939,

v. 36, 90] and consists of the spraying of houses selected because they are thought to be the foci of dissemination of the disease. Selection is principally by the detection of cases among schoolchildren and others emanating from them, special surveys being made for this purpose. Pyrethrum was used until 1944 but was replaced by a single annual application of DDT in oil in 1947, the round being finished by the end of July after failures had demonstrated that application in August was too late. Malaria has become negligible but it is pointed out that it has previously reached very low levels without deliberate control and the results of the spraying campaign are therefore difficult to evaluate. [The abstracter has no doubts of its value.] It is shown that the practice of selective spraying has greatly reduced costs and as cases diminish the number of houses to be sprayed decreases, till in 1953 it had been reduced to 200 only. [This paper may well record the end of the malaria which has long been a pest to Holland, but which has been a source of very valuable epidemiological studies.] *G. Macdonald*

Houel, G. La lutte antipaludique dans les zones rizicoles du Maroc. [**Malaria Control in Rice-Growing Areas in Morocco**] *Bull. Inst. Hyg. Maroc.* 1954, v. 14, Nos. 1/2, 43–90, 8 figs. & 5 pls. [32 refs.]

Rice growing, previously forbidden for health reasons, was introduced into French Morocco in 1949 and a detailed study has been made of its influence on malaria and the control of that disease. It causes an intense proliferation of *Anopheles maculipennis labranchiae* and epidemic malaria associated with elevated parasite and spleen rates for a radius of 5 kilometres around the cultivation areas throughout the 5-month season of irrigation. Control, obligatory from the first, has been to some small extent effected by careful location of plantations away from centres of habitation. Positive control was first carried out by the growers but this proved unsatisfactory and it was taken over by Government. This is still, however, not ideal and an intermediate body responsible would be preferable.

All possible means of antilarval control have been tried, including the application from the air of BHC, DDT, and dieldrin granules, the introduction of DDT emulsion into the water, techniques of water management and biological control by fish, but all have proved unsatisfactory. Particularly notable is the failure of dieldrin granules which caused a proliferation of *A. m. labranchiae* in the treated areas, attributed to its selective effect in killing culicine larvae in the lower water levels where the main concentration was achieved. Imagicidal work has been substituted and DDT at 2 gm. to the square metre is now used exclusively, 2 applications being given in the season. The results have been good. There is a great reduction of adult mosquitoes, the density of larvae has been very much reduced, while parasite rates, spleen rates

and morbidity due to malaria have markedly decreased. There has, however, been no influence on culicines which continue as a major nuisance in the rice-growing areas. *G. Macdonald*

Elliott, R. & Ramakrishna, V. **Insecticide Resistance in *Anopheles gambiae* Giles.** [Correspondence.] *Nature*. 1956, Mar. 17, v. 177, 532–3.

In a pilot scheme on malaria control in Western Sokoto, Northern Nigeria, all the houses in two large communities (Birnin Kebbi and Gwandu) have been treated 3 times since June 1954 at intervals of 6 months with residual sprays of dieldrin. Deposits were of 25 mgm. per sq. ft. except for the third application at Birnin Kebbi which was at 50 mgm. per sq. ft. Since then tests [for technique see this *Bulletin*, 1953, v. 50, 1176] of the susceptibility of wild-caught females or females bred from larvae of *A. gambiae*, from these two places and an unsprayed area, reveal a resistance to dieldrin, but only a questionable resistance to DDT, in mosquitoes from the dieldrin-sprayed areas. The median lethal concentration for dieldrin for mosquitoes from the sprayed areas was 2·0 per cent. which is 8 times the effective concentration for a susceptible London laboratory colony [see Busvine, below]. Specimens from the unsprayed area of Nigeria were all killed at 0·5 per cent., the lowest concentration used, and a median lethal concentration could not be determined. House-flies, which returned to normal numbers in the dieldrin-sprayed zone after the first year of treatment, have a 7-fold increase in resistance to dieldrin. It is possible that the level of resistance to dieldrin in *A. gambiae* may enable the species to withstand the control measures in force. *D. S. Bertram*

Busvine, J. R. **Normal Resistance-Levels of *Anopheles gambiae* to various Insecticides.** [Correspondence.] *Nature*. 1956, Mar. 17, v. 177, 533–4.

Some resistance of mosquitoes to contact insecticides is suspected in certain areas where large-scale residual spraying has been practised. When the increase is slight there is need for careful laboratory tests to determine the range of natural variation in resistance within a species, besides a need for comparisons of specimens from sprayed and unsprayed areas. The determination of natural resistance levels by laboratory tests before spraying campaigns is desirable. Results in tests of this kind, by a method previously described [this *Bulletin*, 1953, v. 50, 1176], are given for *Anopheles gambiae*. Two laboratory strains in London were tested. One originated in Nigeria and the other in Tanganyika. There was no difference in the resistance of the strains to DDT or gamma BHC; the median lethal concentrations were DDT 0·95 per cent., gamma BHC 0·015 per cent. and dieldrin 0·25 per cent. Dieldrin was tested against

the West African strain only. Tests, by another worker using the same test, of adult *A. gambiae* bred out from larvae collected in the field from an unsprayed part of Mauritius indicate a rather greater susceptibility of the Mauritius mosquitoes to DDT (MLC of 0·7 per cent.) but no difference between the West African and Mauritius mosquitoes in resistance to dieldrin. *D. S. Bertram*

Henderson, J. M. **Water Management Planning for Malaria Prevention in the Damodar Valley, India.** *Amer. J. Trop. Med. & Hyg.* 1955, Nov., v. 4, No. 6, 1091–1102, 5 figs.

The Damodar Valley scheme, part of India's new industrial and agricultural development and described as "India's Tennessee Valley", involves the construction of 4 large multi-purpose reservoirs and 2 barrage ponds, as well as a major thermal electric power plant, a power transmission network and the development of irrigation which will benefit about 3 million people. It is in a malarious area immediately northwest of Calcutta where the vectors are *Anopheles culicifacies*, *A. philippinensis* and possibly *A. fluviatilis*. Parasite rates range up to 55 per cent. and spleen rates to 86 per cent., while part of the area to be irrigated is notorious for the social decay which followed the multiplication of malaria there.

Present control is by residual insecticides but more conservative precautionary measures are being advised in the construction owing to the fear that insecticides may not be a permanent answer to India's problem. There are conflicts to be resolved in making the recommendation; measures intended to prevent pool formation when the reservoirs recede may well impede the cultivation of highly valued dry-weather crops; in the lower area to be irrigated the raising of sub-soil water levels may be inimical to the development of *A. philippinensis*, now the local vector, but might on the other hand encourage the development of *A. culicifacies*. The author reviews the scheme, its risks and the conflicts, and proposes a mechanism of compromise and of further research intended to overcome the latter. Research programmes cover additional mosquito dissections; the influence of irrigation on the prevalence of *A. culicifacies*; its influence on ground water tables both locally and generally, and further ecological studies on *A. philippinensis*.

G. Macdonald

Neghme, A., Gutiérrez, J. & Alée, R. **Attempt to eradicate *Anopheles* in the Malaria Zone of Chile.** *Amer. J. Trop. Med. & Hyg.* 1955, Nov., v. 4, No. 6, 1114–18, 1 fig.

The malaria campaign was started in 1937 and was successful before introduction of DDT, no indigenous cases having been diagnosed since 1945. In 1944 house-spraying with DDT was introduced, not only with

the intention of consolidating the gains against malaria but also with that of eradicating the local vector *Anopheles pseudopunctipennis*. The house campaign was reinforced by the spraying of animals with a 0·05 per cent. water emulsion to kill zoophilic mosquitoes, by an elaborate surveillance programme to detect larval and adult mosquitoes and by an antilarval programme where they were found. There were 10 valleys concerned and by 1947 all but 2 had been cleared, while the last record of an adult *A. pseudopunctipennis* was made in 1948. There have, however, been occasional catches of small numbers of immature larvae of this species. They have been along the route followed by traffic from Peru and in the neighbourhood of the frontier with that country. It is assumed, partly on the basis of observation, that mosquitoes are passively transported and also that they actively follow trains of muleteers, and that in consequence constant reintroduction is occurring. Permanent eradication involves international agreement and also ecological changes making the country unsuitable as a focus of development.

G. Macdonald

Pinto, S. C. F. Interrupção de transmissão de malária no Distrito Federal. [**Cessation of Malaria Transmission in the Federal District**] *Rev. Brasileira Malariologia*. Rio de Janeiro. 1955, Jan., v. 7, No. 1, 71–80. English summary.

Earliest records refer to the high incidence of malaria in the Federal District, Rio de Janeiro. In this paper the author describes the malaria control measures that have been vigorously pursued since 1942. Up to 1947 measures taken against the anopheline vectors, *A. tarsimaculatus* and *A. albitarsis* were confined to the widespread application of larvicides and minor engineering works. Considerable success was achieved. In 1947, 3,038 cases of malaria were recorded compared with 7,685 in 1942. In 1948 DDT spraying of houses was begun once a year, with a dosage of 2 gm. of DDT per square metre of surface treated. The number of malaria cases confirmed by microscopic examination in 1948 was 1,626 and in the 3 following years 414, 140 and 42, respectively. In 1952 the frequency of house spraying was increased to twice a year: malaria cases numbered 7 in 1952, 3 in 1953, and nil in 1954.

Norman White

Sá, A. de C. Da influência das variações de nível d'água e do DDT sôbre a produção do *A. darlingi*. [**The Effect of Altering the Level of Water in a Dam and of Residual Spraying with DDT on the Breeding of *Anopheles darlingi***] *Arquivos de Hig. e Sáude Pública*. S. Paulo. 1954, June, v. 19, No. 60, 47–72, 3 charts. [10 refs.] English summary.

In the region of Ribeirão das Lajes (State of Rio de Janeiro), a large hydro-electric plant has been under construction and operation since

1937. Considerable attention was paid to protecting the numerous workmen from malaria and other diseases. Protection from malaria in the early years was done by clearing debris and vegetation from the edges of the dam, which reduced breeding of *Anopheles darlingi*, the sole vector. Since 1945 DDT has been used for house spraying, at first twice yearly, but from 1953 only once a year. The reduction of anophelines and of malaria was distinct but not complete. However, from 1949 onwards the level of water in the lake was reduced (though not regularly). This produced a very marked decline of anopheline breeding, apparently by exposing bare areas, free of vegetation, round the margin of the lake. This effect (which is clearly related to the periodic declines in water level) was more marked with *A. darlingi* than with other mosquitoes. The result was a virtual elimination of *A. darlingi* from houses and complete absence of new cases of malaria since 1949.

The paper includes numerous charts and tables. *J. R. Busvine*

Rodhain, J. & Dellaert, R. Contribution à l'étude du *Pl. schwetzi* E. Brumpt (3me note). L'infection à *Plasmodium schwetzi* chez l'homme. [**Contribution to the Study of** *Plasmodium schwetzi*. **(3rd note.) Infections of** *Plasmodium schwetzi* **in Man**] *Ann. Soc. Belge de Méd. Trop.* 1955, Dec. 31, v. 35, No. 6, 757–75, 4 graphs.

The authors previously reported the successful infection of man with *Plasmodium schwetzi* from chimpanzee blood [see this *Bulletin*, 1955, v. 52, 957]. They now give further information about this subject. The source of the strain was a chimpanzee from Wamba, Belgian Congo. It was inoculated into a young chimpanzee in Antwerp and from this animal intravenously into a man who showed a light infection lasting 32 days. This human infection was then passed successfully to a further 8 people, to 3 *via* another chimpanzee. Four temperature charts accompany the paper and illustrate the mild nature of the fever. A maximum of 14 paroxysms was observed and in several cases practically no fever occurred; all the infections save one terminated spontaneously. No enlargement of the spleen was detected. The person who had most fever showed the usual alteration in the plasma proteins, but little anaemia or marrow changes. After cure, two patients were infected with the Madagascar strain of *P. vivax* to which one responded normally, the other exhibited a modified reaction suggesting that the immunity produced by the chimpanzee parasite may sometimes confer a partial resistance to the human *P. vivax*. In no cases were parasites numerous in the blood, nor, even after 4 or more passages through man, was the virulence enhanced; gametocytes were rare, and successful infection of mosquitoes was apparently not obtained. The loss of the strain has prevented further work.

The authors still feel that *P. vivax* and *P. schwetzi* represent separate species. *P. C. C. Garnham*

GREENBERG, J. **Differences in the Course of** *Plasmodium berghei* **Infections in some Hybrid and Backcross Mice.** *Amer. J. Trop. Med. & Hyg.* 1956, Jan., v. 5, No. 1, 19–28, 5 figs. [15 refs.]

In a series of previous papers [this *Bulletin*, 1956, v. 53, 406] the author and his associates dealt with variations in the resistance to infection with *Plasmodium berghei* among inbred strains of mice, their hybrids and backcrosses. They also studied the pathological changes in various genetic groups of mice, and found that the proportion of mature and immature erythrocytes invaded by the parasite in long-lived and short-lived mice was different. The present investigation was devised in order to ascertain whether there was any relationship between the degree of infection of mature red cells at the end of the 1st week, and the probability that the mice might die of toxaemia during this period.

For this purpose the following groups of mice were used (duration of infection in days shown in brackets): (a) not inbred Swiss strain (8), (b) (c) hybrids of inbred strains (STR = 25, LAF = 20), and (d) backcross (13). The mice were inoculated intravenously and the results were assessed by daily examination of blood films stained by Giemsa's method, in which the following data were recorded: total percentage of parasitaemia, percentage of infected mature and immature red cells [RBC's], percentage of erythrocytes which were immature, and total red cell count.

It was found that infection of mature RBC's reached a peak in a fortnight, after which it dropped to a low level. In polychromatophilic cells the infection increased rapidly, reaching a density of 90 per cent. in 4–6 days. During the 1st week the proportion of immature cells to total number of RBC's rose to 60 per cent. The total parasitaemia observed is built up by an initial peak of infected mature erythrocytes, followed by an increase in infected immature cells. Practically in all the mice the total red cell count began to fall 3–4 days after inoculation. The course of infection in mature erythrocytes (= mean count on 7th day per cent.) varied in the different groups of mice as follows: Swiss 51, backcross 21, LAF 11, STR 6. The general conclusion from these observations is that "the higher the infection in mature erythrocytes, the shorter lived the mice". *C. A. Hoare*

TERRY, R. J. **Transmission of Antimalarial Immunity** (*Plasmodium berghei*) **from Mother Rats to their Young during Lactation.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1956, Jan., v. 50, No. 1, 41–6, 4 figs. [18 refs.]

Experiments are described which clearly illustrate certain immunity phenomena in suckling rats exposed to infection with the RSVP strain of *Plasmodium berghei*. The mother rats were thoroughly immunized, were then mated, and the litters were inoculated with a standard dose

of 2 million parasites given intraperitoneally, at various intervals after birth. After 22 days the incubation period was delayed for about 3 days as compared with a control group born of non-immunized mothers; the later course of parasitaemia and the mortality rates were largely unaffected. Litters 12 days old were less protected, the incubation period being prolonged by only a single day, but rats infected 7 weeks after weaning reacted exactly like the controls. Thus the antibodies in the milk have a cumulative effect during the lactation period and disappear after weaning. The antibodies were proved to be contained in the milk by exchanging litters of immunized and non-immunized mothers: exposure to infection resulted in the baby rats of the normal mother, but suckled by immune mothers, being protected. Thus there is slight or no intra-uterine transmission of immunity.

Finally, serum from immune mothers was given to normal litters (0·5 ml. daily for 10 days before inoculation of *P. berghei*) which were then infected. If the serum was administered to rats 7 days old, it had a marked protective action, sometimes even entirely suppressing the infection; if given to rats 22 days old, however, it had no effect, and the parasitaemia was similar to that of the controls. This suggests that, by the age of 22 days, the rat gut is either impermeable to the large protein molecule which represents the antibody, or contains an enzyme which destroys this substance. The author points out that only young rats and mice possess this ability to absorb antibodies through the gut; human babies are unable to, and transference of maternal antibodies in the latter probably occurs *in utero* [see also Bruce-Chwatt and Gibson, below].

P. C. C. Garnham

Bruce-Chwatt, L. J. & Gibson, F. D. **Transplacental Passage of *Plasmodium berghei* and Passive Transfer of Immunity in Rats and Mice.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1956, Jan., v. 50, No. 1, 47–53, 2 figs. on 2 pls. [14 refs.]

Earlier work by Bruce-Chwatt [see this *Bulletin*, 1954, v. 51, 884] on the rarity of congenital *Plasmodium berghei* malaria was confirmed by a further series of experiments in which 13 gravid white mice and 10 gravid rats were infected with about 40 million parasites 5 to 10 days before delivery. The births were normal in all but 3 mice; congenital transmission was observed in the litters of 2 of the latter—in one after Caesarian delivery, in the other in the litter of a mother that died shortly after she had given birth. Histological examination of heavily infected placentas was made but failed to show why penetration of the unicellular barrier between the maternal and foetal circulations was so difficult. [The sections were apparently from cases where transplacental infection had not occurred; it might have been valuable to compare them with material from the two positive cases.]

The second part of the enquiry was devoted to the transmission of maternal immunity to the offspring, and the authors point out that the mechanism of such transmission varies in the different mammals: the immunity in ungulates derives chiefly from the colostrum and milk, in man, rabbit and guineapig transplacentally, and in rats and mice from both sources. Five female rats were immunized during pregnancy by 8 inoculations of *P. berghei* and again after delivery. The litters were challenged with a dose of 50,000 parasites at about the age of 16 days and a control series was treated similarly. The difference was remarkable and much greater than that observed by Terry [see above] who used larger challenging doses. Only 2 baby rats out of 23 contracted the disease, the prepatent period was double the normal and the parasitaemia less than one-tenth. Interchange of baby rats born of immunized and normal mothers showed that the immunizing factor is contained in the milk, though a second and less effective factor had been transmitted *in utero*. Finally, baby rats were inoculated with immune serum—0·1 ml. before infection, 0·2 ml. after infection, and subsequent doses of 0·15 ml. at 2-day intervals; 11 out of 14 rats contracted the disease and 10 died, but the prepatent period was delayed for 4 days and the rats survived longer than the controls. *P. C. C. Garnham*

Sautet, J. Influence du vin et de l'alcool sur le traitement des affections à *Plasmodium berghei* chez la souris. [**Influence of Wine and of Alcohol on the Treatment of** *Plasmodium berghei* **Infections in Mice**] *Bull. Acad. Nat. Méd.* 1956, v. 140, Nos. 9/10, 154–5.

Different batches of mice were placed on the following diets and their weight curves were studied: bread and water; ordinary diet plus milk in varying amounts; ordinary diet plus red wine (0·018 gm. alcohol daily); ordinary diet plus 0·08 gm. alcohol. After 16 days on these diets, the greatest increase in weight occurred among the milk drinkers, the least among the wine drinkers. Next, similar observations were made on mice exposed to *Plasmodium berghei*. Mice on alcohol died more quickly than those on an ordinary diet; if the infections were damped down with a little quinine, the addition of red wine in excess to the diet again caused quicker death. It is assumed from these experiments that red wine interferes both with growth of mice, and, if taken in sufficient quantity, with the treatment of malaria. *P. C. C. Garnham*

Demina, N. A. [**Tissue Stages of** *Plasmodium relictum*] *Med. Parasit. & Parasitic Dis.* Moscow. 1956, v. 25, No. 1, 48–54. [Numerous refs.] [In Russian.]

The author describes observations on a strain (S) of *Plasmodium relictum*, which had been isolated near Moscow in 1952 from the great tit,

Parus major, and has been maintained by passages through siskins (*Spinus spinus*) and redpolls (*Acanthis canaria*). The exo-erythrocytic (EE) development of the parasite was studied in birds inoculated intramuscularly with the blood and organ suspensions of infected donors, as well as with sporozoites.

In birds inoculated with erythrocytic parasites and examined between the 5th and 42nd days EE forms were detected only from the 23rd day onwards. Among the birds inoculated with sporozoites and examined between the 10th and 28th days EE forms were present in practically 100 per cent., while in those inoculated with organ suspensions and examined between the 6th and 14th days—when parasitaemia was present —EE forms were found in 75 per cent. In another experiment, birds, which were infected with the blood of donors whose organs contained numerous EE forms, were examined between the 7th and 17th days, during the acute phase of the infection: EE stages could be found only from the 11th day onwards. From birds infected with sporozoites, an EE line was successfully maintained through 25 passages, by inoculation of organ suspensions of the donor.

The EE forms of *P. relictum* (strain S) were morphologically like those of *P. gallinaceum*. EE schizonts and merozoites packed the brain capillaries, but were especially numerous in the liver, spleen and lungs.

In view of the ease with which EE forms of *P. relictum* can be obtained and propagated by passages through siskins and redpolls, this parasite and its hosts provide suitable material for the study of diverse malariological problems. *C. A. Hoare*

TRYPANOSOMIASIS

In this section abstracts are arranged as far as possible in the following order:—African—*human, animal;* American—*Chagas's disease and other trypanosome infections. In each form the following order is followed*:—*epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.*

See also p. 942, East Africa High Commission. **East African Tsetse and Trypanosomiasis Research and Reclamation Organization. Annual Report 1954–55.**

Spezzaferri, F. Storia della malattia del sonno. [**The History of Sleeping Sickness**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1956, Mar., v. 37, No. 3, 136–45. [21 refs.]

Lovemore, D. F. **A Preliminary Report on the Results of Blood Meals from Tsetse collected at Kariangwe-Lubu River Valley: June 1951 to May 1952.** *Bureau Permanent Interafricain de la Tsé-Tsé et de la Trypanosomiase No. 208/0* [Léopoldville (Congo Belge)]. 1955, Oct. 22, 5 mimeographed pp.

This mimeographed report, circulated to workers on tsetse and trypanosomiasis problems, places on record the results of the identification of the blood meals from 200 specimens of *Glossina morsitans* collected in a locality in the Zambesi valley, in the Sebungwe District of Southern Rhodesia. The area is one where the tsetse have been virtually undisturbed and where game animals are numerous; the results can therefore be assumed to show the hosts of this tsetse under natural conditions. These results are given in a table which shows nearly half (40·5 per cent.) of the feeds to have been on pig, either wart-hog or bush-pig. This interesting result is paralleled in other areas [see this *Bulletin*, 1956, v. 53, 416].

A feature worthy of note is that impala, which were numerous in the area, do not seem to have been used as food to any great extent, only one blood meal on this species having been identified. [The suggestion that the feeds on " unidentified bovids possibly sable antelope " and " unidentified bovids " might have been impala cannot be supported, as the identification tests were carried out in such a way that the possibility is excluded. It is, however, possible that the 10 meals which were ascribed to " unidentified bovids " because the samples of blood provided were not sufficient, or were too far digested, to allow a more precise identification, could be distributed among the specified bovids in the proportions these had been shown to occur, but this would only increase the number of impala fed on from 1 to 2.] Failure of this tsetse to use buffalo is also noteworthy. The author suggests that this may be because these animals are too much on the move to form a dependable source of food for the fly. It is also interesting, in view of the commonly held belief that the baboon forms an important source of food for the tsetse, that this animal, although numerous, did not figure among the identifications. [Again, the suggestion that the feed on a monkey might have been on a baboon cannot be supported; the tests as applied would have differentiated between these two animals.]

The degree to which these identifications show *G. morsitans* to feed on elephant and rhinoceros (6 per cent. each) is important, in view of the doubts which have been expressed as to whether these pachyderms are fed on by tsetse at all.

[All these results, which may come as a surprise to some, suggest to the abstracter the importance now of combining these identifications of the tsetse's blood meals with observations on the relations between the patterns of behaviour of the tsetse and their hosts; until such studies have been made, a full understanding of the tsetse's food habits and requirements will be difficult.] *W. H. Potts*

Maillot, L. & Taufflieb, R. Présence de *Glossina nashi* Potts 1955 en Afrique Equatoriale française. [**Presence of *Glossina nashi* in French Equatorial Africa**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 6, 847–8.

Gall, D., Hutchinson, M. P. & Yates, W. **The Estimation of Cerebrospinal-Fluid Protein in Sleeping Sickness: Sicard and Cantaloube's Method and a Sulphosalicylic-Acid Method.** *Ann. Trop. Med. & Parasit.* 1955, Dec., v. 49, No. 4, 419–28, 3 figs.

A standardized technique, based on the Sicard and Cantaloube method, is described for the estimation of protein in cerebrospinal fluid. It gives more consistent results than the original technique. The accuracy is within ±5 mgm. at the 95 per cent. confidence level, but can be improved by eliminating tube differences, standardizing bore and controlling calibration error. The Sicard and Cantaloube method has a sensitivity of only about half a mgm. per true mgm. The reading is correct at about 20 mgm. per 100 ml.; at lower levels the reading is high, and at higher levels low.

The Medical Research Council grey-wedge photometer may be used in conjunction with a sulphosalicylic acid turbidimetric method, which is described. It gives nearly true readings in mgm. protein per 100 ml. direct from the scale of the instrument and has an overall accuracy about double that of the Sicard and Cantaloube method. Further, it requires only 1 ml. of cerebrospinal fluid instead of 4 ml., involves no heating and can be read in 5 minutes as opposed to 5 hours.

J. H. Birkinshaw

Roubaud, E. Les précurseurs dans la lutte contre la maladie du sommeil en Afrique Noire française (1908–1930). [**Early Workers in the Control of Sleeping Sickness in the French African Territories (1908–1930)**] *Rev. Med. et d'Hyg. d'Outre-Mer.* 1956, Mar. 15, v. 28, No. 244, 48–54. [Refs. in footnotes.]

Anderson, E., Saxe, L. H. & Beams, H. W. **Electron Microscope Observations of *Trypanosoma equiperdum*.** *J. Parasitology.* 1956, Feb., v. 42, No. 1, 11–16, 10 figs. on 2 pls. [15 refs.]

Galvão, A. B. Chave para as espécies brasileiras do gênero *Triatoma* Laporte, 1833 (Hemiptera, Reduviidae). [**Key to the Brazilian Species of *Triatoma***] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, July, v. 7, No. 3, 343–5.

The English summary appended to the paper is as follows:—

"To help the work of the technicians in entomology of the Serviço

Nacional de Malária in the rapid determination of the Brazilian species of the genus *Triatoma* Laporte, the author constructed a key mainly based on the informations contained in the book of Professor Costa Lima 'Insetos do Brasil', vol. II (Hemiptera). Thus, he omitted the species never described in Brazil as well as the ones already considered as synonyms but included those species lately described. The key includes the species *rubrofasciata*, *infestans*, *rubrovaria*, *sordida*, *tibiamaculata*, *brasiliensis*, *brasiliensis melanica*, *vitticeps*, *petrochii*, *arthurneivai*, *oliveirai*, *matogrossensis*, *melanocephala*, *maculata* and *wygodzinskyi*."

Trindade, C. I., Brant, T. C. & Lopes, G. G. Oito casos da forma aguda da Doença de Chagas, no Município de Encruzilhada do Sul, Estado do Rio Grande do Sul. [**Eight Cases of the Acute Form of Chagas's Disease in Encruzilhada, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, July, v. 7, No. 3, 371–3, 1 fig.

The English summary appended to the paper is as follows:—

"The authors describe eight cases of the acute form of Chagas' disease observed by them in the county of Encruzilhada, state of Rio Grande do Sul. All cases presented edema of the eyelids and were positive for *Schizotrypanum cruzi*."

LEISHMANIASIS

In this section abstracts are arranged as far as possible in the following order:—visceral, cutaneous, muco-cutaneous.

Pessoa, S. B., da Silva, L. H. P. & Figueiredo, J. Calazar endêmico em Jacobina (Estado da Bahia). [**Endemic Kala Azar in Jacobina, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, Apr., v. 7, No. 2, 245–50.

The English summary appended to the paper is as follows:—

"The authors report a brief excursion to Jacobina, state of Bahia, where they found an endemic focus of kala-azar. Out of 31 cases found, in 7 the diagnosis was made by means of sternal puncture, in 15 by the formol-gel test, and the rest by clinical examination. They emphasize the necessity of carrying out surveys in localities of the state of Bahia with a topography similar to that of Jacobina, i.e., in the vicinity of mountains, between valleys called 'grotões', as Morro do Chapéu, Campo Formoso, Saúde and others."

Li Moli, S. Sul trattamento con glucantim della leishmaniosi viscerale infantile. [**Treatment of Kala Azar in Children with Glucantime**] *Giorn. di Malattie Infettive e Parassit.* Rome. 1956, Jan., v. 8, No. 1, 14–19. [19 refs.]

The following is a translation of the author's summary:—

The author describes and comments on the results of treating children suffering from leishmaniasis with Glucantime in the Children's Clinic in Bari between 1949 and 1954.

Glucantime, used in a much lower dose (25–30 mgm./kgm.) than that commonly employed (50–100 mgm./kgm.), was given on alternate days for a single schedule averaging 20 injections.

Of 20 children treated, 16 were cured, 2 died (one from inherent intolerance to Glucantime) and 2 abandoned treatment.

H. J. O'D. Burke-Gaffney

Pifano C., F., Medina, R., Medina Febres, M. & Romer, M. La Leishmaniasis tegumentaria americana. [**American Dermal Leishmaniasis**] *Rev. Sanidad y Asistencia Social.* Caracas. 1954, Sept.–Dec., v. 19, Nos. 5/6, 403–23. [18 refs.]

The English summary appended to the paper is as follows:—

" The authors present a review about the actual status of Tegumentary Leishmaniasis in Venezuela. Considering mainly the epidemiological, clinical, histopathological aspects and diagnosis.

" The disease has a wide geographical distribution in the country, especially in moist and woody zones. It is endemic in wild regions and it is possible that may exist selvatic reservoirs of the protozoa. There are epidemiological basis to suspect that Phlebotomus panamensis, Shannon 1926 could be one of the vectors.

" Reference is made about the clinical aspects of leishmaniasis describing: cutaneous forms with the framboesiform, sporotrichoid, chromoblastomicoid, pyodermoid, syphiloid, epitheliomatoid and leproid varieties; and mucous forms (nasobucco pharyngeal) considered as a late manifestation of the disease, always preceded by the cutaneous form.

" Histological alterations are described that have been formed in typical cases of the disease, which do not offer any specificity.

" Diagnosis is made on the basis of clinical, and epidemiological data, recommending in order of importance: apposition smears, ' leishmanin ' dermal—reaction and cultures in special media—The ' leishmanin ' intradermo-reaction is considered the method of choice because of its simplicity and high grade of specificity. The antigen used is a parasite suspension obtained from culture in phenolized (0·4%) physiological solution.

" Concerning treatment, tartar emetic and other antimonial compounds continue offering the only chemotherapeutic possibilities up to date. It is

suggested that it is necessary to intensify the investigation in this matter.''

León, L. A. La *Leishmania brasiliensis* Viana, 1911 y las Leishmaniasis Otorrino-buco-faringolaríngea y oftálmica. [*Leishmania braziliensis* **and the Ear, Nose, Throat and Eye Manifestations of Leishmaniasis**] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1954, Jan.–Apr., v. 2, Nos. 1/2, 15–28, 14 figs. on 4 pls. [21 refs.] English summary.

FEVERS OF THE TYPHUS GROUP

In this section abstracts are arranged as far as possible in the following order:—general; louse-borne typhus, flea-borne typhus, mite-borne typhus; rickettsialpox; tick-borne typhus; Q fever, other rickettsial diseases.

Bogacz, J. Contribution à la chimioprophylaxie du typhus expérimental. [**Studies of Chemoprophylaxis of Experimental Typhus**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 4, 511–43, 2 text figs. & 8 figs. on 4 pls. [45 refs.]

The experiments here recorded were carried out with a single strain of *Rickettsia prowazeki*, HSP [*Historique Souche Pulmonaire*], which had been adapted to rabbit lungs by intratracheal passage. Details of the preparation and preservation of standard samples of virus in dried lungs are given at length.

The large number of chemotherapeutic agents tested included the antimalarial drugs Atebrin [mepacrine], alum, Malocide [pyrimethamine] and 2616 RP (p-aminobenzene sulphamide-2 pyrimidine); trypanocides such as suramin and tryparsamide; the antibacterial agents—sulphonamides, aureomycin and erythromycin; the antiviral compound lithium antimoniothiomalate [anthiomaline]; product 2836 (bis-(*p*-nitrophenyl)-1-1 trichloro-2-2-2 ethane) known to be active against rickettsiae together with chemically related substances.

In the first group of experiments rabbits were infected intracutaneously. Chemotherapy was begun about half an hour later by subcutaneous injection. The size of the nodule and the presence or absence of necrosis were compared in treated and control animals. In no case was infection completely arrested but 4 compounds showed considerable activity. The most active was the antirickettsial compound, product 2836, next in order of activity was a related compound 2975 (bis-(*p*-aminophenol)-1-1 ethane), then Malocide and the compound G (bis-(*p*-methioxy-phenyl)-1-1-propane).

These 4 compounds were also tested in mice inoculated intranasally with the same strain of *Rickettsia*. Treatment by subcutaneous injection was started 24 hours before infection and continued for 3 days afterwards. On the fifth day all animals were sacrificed and portions of lung showing hepatization examined microscopically for rickettsiae. In all control animals very large numbers of rickettsiae were seen, whereas in those treated with compounds 2836 and 2975 very few organisms were present. Animals treated with Malocide and compound G gave intermediate results.

Finally 2 rabbits were inoculated intracutaneously at a number of different sites with enormous doses of rickettsiae in mouse lung with and without each of the 4 above-mentioned compounds. Two and 4 days after inoculation the size of control nodules was compared with those where organisms plus drug had been injected together. Rickettsiae plus product 2836 or 2975 gave tiny nodules at 2 days which had disappeared by the fourth day. All control sites showed large necrotic nodules on both days. With Malocide and product G small nodules developed but were not necrotic. *Mary Barber*

YELLOW FEVER

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, transmission, pathology, diagnosis, clinical findings, treatment, control.

Pan American Sanitary Bureau. **Yellow Fever Conference, 21–22 December, 1954.** *Amer. J. Trop. Med. & Hyg.* 1955, July, v. 4, No. 4, 571–661, 9 maps.

A verbatim record is presented of a conference convened to review the present state of yellow fever in the Americas (including Trinidad), attended by many with special experience and proceeding without set papers. The Chairman, F. L. Soper, gave a historical account well illustrated by maps leading to the present wave-like epizootic in the Central Americas. Discussion covers almost all aspects of the disease with considerable emphasis on the gaps in the knowledge of epidemiology and control and of the administration of quarantine and research. M. Theiler discussed the epidemiological and immunological aspects of the virus, describing its association as revealed by the haemagglutinin test with a number of others, and discussing the possibility that the distribution of the disease might be influenced by cross immunity, as has quite possibly been the case in Egypt where West Nile virus is prevalent. The known reservoir lies in monkeys of 3 genera, *Cebus*, *Alouatta*, and *Ateles*; the first is widespread in continental south America and does not commonly die when infected with yellow fever virus which is, however,

usually fatal to the last two species prevalent in the isthmus and in central America. The rapid re-birth of a non-immune potential reservoir in the south and its very slow evolution after the fatal epidemics in the north markedly influenced the epidemiology of the disease. The accepted mosquito vector in Central America is *Haemagogus spegazzinii falco* but little is known of its habits. It is thought to be a tree-hole breeder but extremely few larvae have been recovered in nature, and no males have been captured in the field though one has been seen. H. Trapido notes that monkeys dying of yellow fever do so in areas not infested by this mosquito, and that the virus has not been recovered from it despite elaborate search. He considers that other species, perhaps *Haemagogus equinus*, must be considered, and J. Boshell considers that even *Phlebotomus* must be re-examined. Boshell points to the recrudescence of monkey epidemics after long dry periods in the apparent absence of any *Haemagogus* species, and considers that other reservoirs and particularly the marsupial should be re-examined with care. However, even if the traditional picture is accepted it is disturbed by the periodic waves in prevalence of *Haemagogus* noted by Trapido, the coincidence of which with the appearance of virus has facilitated its passage across areas which would otherwise constitute barriers. This may have happened recently in Panama. In consequence of these uncertainties, and although N. W. Elton has been able to predict the routes of the simian epidemic with considerable accuracy, the limit of spread is not reasonably predictable.

Soper and others emphasize the importance of jungle yellow fever to the rural population, for whom vaccination cannot constitute a complete protection, and note that passage from the jungle to the town has been recorded some 20 times. Initial cases in epidemics, whether rural or urban, are rarely recognized, diagnosis of even formal autopsy material presenting considerable difficulty to non-specialized pathologists, and control should turn on the recognition of risks rather than await the notification of cases. The protection of towns still lies in *Aëdes* eradication, the progress of which throughout the Americas is described and illustrated by Soper, and the lack of which in Port of Spain, Trinidad, led to the infestation of that port, the first such maritime port infestation for many years. The circumstances of this outbreak, which led to grave financial loss for Trinidad, and of the occurrences in rural parts of that country, are described by W. G. Downs. Such urban outbreaks are the principal potential cause of maritime transmission, and America has the chief reason to fear this, though the chief international expression of concern arises in Asia. The quarantine mechanism came in for considerable criticism. It was considered that the danger lies in the occurrence of jungle yellow fever in the neighbourhood of towns with a high *Aëdes* index, and information on the latter subject is now included in the Pan American Sanitary Bureau bulletin. The danger lies in these "risk areas" which should properly be the subject of quarantine and

not entire countries such as Brazil in which the disease has been known to occur. Despite discussion, no acceptable definition of "risk areas" was presented.

Research and pathological study have for long been based on a Rockefeller laboratory in New York and 3 laboratories in the yellow fever areas. The first of these has now closed. There was much discussion on the policy of research in which the need for a base laboratory such as that which has now closed was emphasized, and the question was raised whether further decentralization of laboratories was desirable. Boshell considered emphatically that mobile units should be established to be located in the path of advancing epizootics so that adequate entomological, mammalogical, virological and epidemiological studies could be made when they arrived. There was general agreement that research was a matter for all countries of the continent and not only for those affected at any one time, and that it should be organized on the principle of long-term study rather than examination of immediate difficulties.

G. Macdonald

Leví-Castillo, R. *Haemagogus soperi* n.sp. mosquito trasmisor de fiebre amarilla selvática en el Ecuador (Diptera-Culicidae). [*Haemagogus soperi* **n. sp., a Vector of Jungle Yellow Fever in Ecuador**] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1954–1955, v. 2, Nos. 3/4, 479–84, 8 figs. [12 refs.] English summary (7 lines).

Smithburn, Kenneth C.; Durieux, C.; Koerber, R.; Penna, H. A.; Dick, G. W. A.; Courtois, G.; de Souza Manso, Caio; Stuart, George; Bonnel, P. H. **Yellow Fever Vaccination.** *World Health Organization Monograph Series No. 30.* 238 pp., numerous figs. 1956. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [25s.; $5.00; Sw.fr. 15.–.]

In the first chapter of this publication Smithburn outlines the basic principles of yellow fever immunization, discusses the establishment of active and passive immunity and indicates the use of immunological methods in the diagnosis of the disease, in the identification of the causative virus and in immunity surveys undertaken to define the distribution and prevalence of the natural infection. Subsequent chapters, by various authors, deal with the vaccines prepared from different immunizing strains of virus, with the time of appearance and duration of the immunity conferred by such vaccines, with the problem of mass immunization, with post-vaccination reactions and with the international regulation of yellow fever vaccination.

In the chapters devoted to vaccines and vaccine techniques Durieux gives details of the procedure followed at the Pasteur Institute, Dakar,

for the production and administration of vaccine developed from the French strain of virus, modified by serial brain-to-brain passage in white mice. This Dakar vaccine, which since 1939 has been applied by cutaneous scarification, is now, as it has been since 1946, prepared from the French strain at its 258th–260th mouse passage and is stored in ampoules in the form of dried cerebral tissue. At the time of use vaccine is suspended in a solution of gum arabic; three drops of this suspension are placed, a few centimetres apart, on the outer surface of the upper arm and then three scarifications 8–10 mm. in length are made through each of the drops. Vaccine thus administered should have a titre of at least 250,000 MLD per ml. and the individual dose should contain a minimum of 5,000 LD50. Inoculation by scarification makes it possible to combine yellow fever vaccination with smallpox vaccination; this mixed vaccination, by means of which simultaneous immunization against both diseases can be carried out with the minimum of equipment, has been extensively practised since 1940 in the French territories in Africa south of the Sahara. Penna describes the various stages in the preparation and control of the 17D vaccine produced at the Oswaldo Cruz Institute, Rio de Janeiro, and, in a separate chapter, gives particulars of the technique used for its administration in the field. Serial cultivation *in vitro* of the Asibi pantropic strain was shown in 1937 to have resulted in the production of a variant, 17D, characterized by loss of hepatotropism and diminution of residual neurotropic potency. By the use of this modified strain a safe and efficient means of vaccinating human beings against yellow fever had clearly become available. As, however, the titre of virus produced by multiplication in tissue culture is low, vaccine is prepared from developing chick embryos inoculated with culture virus; to this end hen eggs, which on the 9th day of incubation show a viable embryo, are inoculated with 0·06 ml. of 229th to 255th subculture passage material. The final product, a vaccine of the aqueous base, serum-free type, is placed in ampoules, rapidly shell-frozen and desiccated in the frozen state. For use 0·5 ml. of a 1 in 100 dilution of vaccine [*i.e.*, the desiccate of 0·5 ml. of vaccine is diluted into 5 ml. of saline, to make a 1 in 10 dilution, which is further diluted to 1 in 100] is injected subcutaneously near the insertion of the deltoid muscle. Vaccine thus administered should have a titre of at least 200,000 LD50 per ml. and the individual dose should contain a minimum of 1,000 LD50. Dick discusses application of the scarification method to vaccination with 17D. Vaccine prepared by grinding the whole virus-infected chick embryos with gum arabic solution and desiccating the homogenized mixture to powder form has, when reconstituted in distilled water at the time of use, proved to be easy of administration by the scratch technique and capable of producing a level of immunity of the same order as that resulting from subcutaneous inoculation of the virus. For scarification, such a vaccine or one prepared by making a simple crude suspension of infected decapitated chick embryos would not require the strict bacterial sterility

applicable to a vaccine for subcutaneous inoculation and would thus reduce costs in manufacture; moreover the absence of syringes would facilitate mass vaccinations and obviate syringe transmission of disease. Further, since, to afford the same protection, smaller amounts of antigen would seem to be required when administered by scarification than by the subcutaneous route, it is suggested that mass vaccination with 100 mouse intracerebral LD50 of virus should be investigated; were this dose found to be adequate, a 5 ml. ampoule would be sufficient to vaccinate 1,000 persons, thus reducing the cost of vaccination to one-tenth of the present figure. In the interests of economy, investigation into the antigenicity of 17D mouse-brain virus as a scarification vaccine is also advocated.

Two chapters concern the time of appearance and duration of immunity conferred by yellow fever vaccination. Durieux and Koerber, by means of the neutralization test method employed at the Pasteur Institute, Dakar, namely that of mixing the serum to be tested with varying dilutions of the mouse-adapted French strain of virus and inoculating batches of white mice intracerebrally with the mixtures, adduce evidence that, in the sera of persons inoculated with Dakar vaccine by scarification, the presence of antibodies on the 7th to the 9th day is revealed by a progressive increase in the average survival time, and then from the 10th to the 14th day by the definite protection, of mice inoculated with the 1 in 50,000 virus suspension. The protective power then gradually increases, approaching the maximum towards the end of the third week. Duration of immunity among persons vaccinated by the Dakar method and possessing certificates stating the date of vaccination was shown to be as follows: 9 of 10 (90 per cent.) tested 6 years after vaccination proved to be immune, as also were 14 of 16 (87·5 per cent.) tested from 7 to 12 years after vaccination. Courtois, in a study of the immunity conferred by 17D vaccination, observes that neutralizing antibody is present by the 10th post-vaccination day in a high percentage of inoculated persons; thereafter the antibody titre gradually increases to reach a maximum between the 21st and 28th post-vaccination days. Despite the delay in the appearance of demonstrable antibody, however, field experience has shown that the protective effect of 17D vaccination begins not later than one week after inoculation. To determine the duration of immunity this author in 1953 examined the sera of 79 persons, whom administrative documents proved to have been vaccinated in 1941. Results showed immunity to have been maintained in 76 (96·2 per cent.) of these persons for a period of 12 years.

Chapters on mass vaccination in Africa and in South America are contributed by Durieux and by de Souza Manso, respectively. Large-scale vaccination has been practised since 1934 in French territories south of the Sahara, first by subcutaneous inoculation of Laigret's French neurotropic virus vaccine and since 1939 by scarification with Dakar vaccine. By the end of 1953 the number of vaccinations had exceeded 56 million. Each inhabitant of these territories, where the population

is about 25 million, may be assumed, therefore, to have been vaccinated twice. The success of such vaccination is reflected in the decrease in the number of yellow fever cases from 134 in the period 1934–38 to 5 in the period 1949–53. De Souza Manso describes the system of mass vaccination applied in Brazil, where between 1937 and 1954 nearly 22 million persons in 1,350 counties have been inoculated with 17D vaccine. The influence of this measure on the spread of jungle yellow fever is also discussed; even in counties, the geographical situation and the vegetation of which particularly favour the occurrence of future epizootic outbreaks, vaccination of 70 per cent. of the inhabitants is considered to offer a good security margin, particularly when it covers mostly a rural population.

In the chapter on post-vaccination reactions Stuart gives an account of the development of immunizing strains of yellow fever virus, of the various vaccines prepared from these strains and of the types of reaction which have been reported to follow the administration of such vaccines to man. Reactions, in varying number, type and degree of severity, are shown to have complicated the application of practically all methods of yellow fever immunization, irrespective of the immunizing strain in the vaccine employed. Reactions are classified according to whether or not they have involved the central nervous system, and their occurrence in these categories is recorded separately, under each of the various immunizing methods. The aetiology of both categories of reaction is fully considered.

In the concluding chapter Bonnel indicates the international regulations governing yellow fever vaccination and the conditions under which a valid international certificate may be issued. This author also details the responsibilities of the World Health Organization in connexion with the approval and control of yellow fever vaccines.

Finally, a classified bibliography is provided to enable workers to consult recent literature on the subjects dealt with in the Monograph.

G. Stuart

RABIES

Coonoor. **The Pasteur Institute of Southern India, Coonoor. Annual Report of the Director 1954** [Veeraraghavan, N.] **and Scientific Report 1955.** 73 pp., 2 charts. 1956. Madras: Diocesan Press.

Most of the subject-matter of this publication is concerned with rabies. In the Director's report the results of anti-rabies treatment administered at the Institute and its subsidiary centres during 1954 to 23,424 persons are given in detail. The vaccine employed was a 5 per cent. suspension

of infected sheep brain (Paris strain of fixed rabies virus) in distilled water (DWV) or in normal saline (SV) prepared by Semple's method. Of 17,926 persons, for whom complete statistical data are available, 10,655 received complete treatment: 8,212 with DWV and 2,443 with SV; and 7,271 were incompletely treated: 4,637 with DWV and 2,634 with SV. The number of deaths among those treated may be summarized as follows: 21 (0·12 per cent.) among 17,926 who received complete or incomplete treatment with either DWV or SV; 4 (0·048 per cent.) among 8,212 completely treated with DWV; 2 (0·08 per cent.) among 2,443 completely treated with SV; 4 (0·08 per cent.) and 11 (0·42 per cent.) among those incompletely treated with DWV and SV, respectively. All 21 deaths followed dog bites and occurred among Asian patients. Among 12,974 persons treated with DWV there were 3 cases of neuroparalytic accident, *i.e.*, 1 in 4,325, while among 5,129 treated with SV there was no case. (In the period 1933–54 only 13 persons treated with SV developed such accidents, *i.e.*, 1 in 23,201). In view of the comparatively high incidence of these accidents complicating treatment with DWV, issue of this vaccine was discontinued from 1 November 1954.

In the Scientific Report Veeraraghavan comments on the value of 5 per cent. Semple vaccine in human treatment, basing his assessment on the comparative mortality among the treated and the untreated. From observations made between 1946 and 1954 it is shown that among 213 persons, who were bitten by animals whose infectivity was proved by the death from rabies of one or more of the persons or animals bitten (classified as Group I) and who received a complete course of treatment with SV, 16 (7·5 per cent.) died of rabies, while of 85 who remained untreated after similar exposure, 36 (42·3 per cent.) succumbed to that disease. Treatment would appear, therefore, to save 5 out of every 6 persons who would otherwise die from rabies. Two articles record the results of investigations made with a view to determining whether or not the substitution of distilled water for normal saline in the preparation of 5 per cent. Semple vaccine results in an increase in the antigenicity of that vaccine. To this end Veeraraghavan traced in 1954 the fate of 50 persons bitten by definitely infective animals (Group I); 2 (6·45 per cent.) of 31, who had received a complete course of treatment with DWV, and 8 (42·1 per cent.) of 19, who had remained untreated, died of rabies. With the same object, Veeraraghavan and his colleagues made an experimental determination. In the main experiment 5 groups, each but one comprising 15 guineapigs, were employed. Groups A and B received daily, for 7 days, a subcutaneous injection of 0·3 ml. DWV and SV, respectively, and were challenged on the 8th day. Groups C and D received daily, for 7 days, a subcutaneous injection of 1·0 ml. DWV and SV, respectively, the first injection being given one hour after challenge. Group E was untreated and served as control. Challenge consisted of 0·1 ml. of a 1 in 80 dilution of lyophilized NYC street virus inoculated

intramuscularly; the number of intramuscular LD50 of challenge was 11·3. Deaths from rabies in the 5 groups were: 0 in Groups A and B, 9 (out of 14) in Group C, 11 in Group D and 14 in Group E. Neither the results of human treatment nor the experimental data now presented indicate any superiority of the vaccine prepared in distilled water over that prepared in normal saline.

The same authors report the result of studies made to determine the protective power of hyperimmune anti-rabies serum, when administered by different routes to guineapigs after challenge with lyophilized canine submaxillary gland suspensions of street rabies virus. In the most comprehensive experiment 5 groups of guineapigs, 15 in each group, were challenged with 0·1 ml. of a 1 in 80 dilution of NYC street virus given intramuscularly. Group A received 0·25 ml. serum, intramuscularly, one hour after challenge; Group B 0·25 ml. serum, subcutaneously, 24 hours after challenge; Group C 0·25 ml. serum, infiltrated locally at the site of the virus inoculation, one hour after challenge; Group D served as untreated controls; and Group E received 0·3 ml. Semple vaccine daily, subcutaneously, for 7 days and the challenge on the 8th day. All the animals treated with serum intramuscularly or subcutaneously died of rabies, while 14 of the 15 animals infiltrated with serum at the site of challenge died. In these groups the incubation period was prolonged. One animal in the untreated control group survived; there was no mortality in the vaccinated group. The administration of serum subcutaneously, intramuscularly or into the site of infection, while prolonging the incubation period, had, therefore, no protective value for animals challenged previously with street rabies virus. *G. Stuart*

Laughlin, J. & Ross, D. J. C. **A Case of Rabies in Surrey.** *Lancet.* 1956, Apr. 14, 421–3, 1 fig.

A case of hydrophobia in Britain is a rarity these days; when one does occur it is in a person who has contracted infection in a country where rabies is endemic and who has travelled to the United Kingdom during the incubation period of the disease. The occurrence of such a case in May 1955 is recorded in the present article.

Two months before the onset of symptoms the patient, a 32-year-old male, had, while in Pakistan, been bitten by a dog on the right forearm; the wounding had been superficial and had left no scar. During the patient's illness, from 6 May until the time of his death one week later, the signs, symptoms and clinical course were characteristic of the excited or furious type of rabies. Laboratory examination of the deceased's brain and submaxillary gland confirmed the clinical diagnosis. Sections of the brain showed the perivascular lymphoid-cell collections of encephalitis with, in the hippocampus region, the Negri bodies of street virus rabies.

The virus of rabies was isolated from brain and submaxillary gland alike by mouse inoculation.

In conclusion the authors emphasize the importance of maintaining the 6 months' quarantine period for dogs entering the United Kingdom. [There is ample proof that quarantine for 6 months is justified. Thus, according to Galloway (this *Bulletin*, 1945, v. 42, 674), during a period of 21 years, 16 dogs held in quarantine developed rabies between 1 day and 6 months after importation into England.] *G. Stuart*

Cajal, N. & Mateescu, S. Diagnostic rapid al turbării cu ajutorul microscopului de contrast de fază. [**Rapid Diagnosis of Rabies with the Phase Contrast Microscope**] *Studii şi Cercetări Inframicrobiol., Microbiol. şi Parazitol.* 1955, Jan.–June, v. 6, Nos. 1/2, 35–8, 1 fig. on pl. [14 refs.] French summary.

The following is a translation of the authors' summary:—

The authors describe the diagnosis of rabies in a very short time (about 15 minutes) by examination of frozen sections of Ammon's horn measuring 20 to 50 μ by means of the phase contrast microscope after fixation in Dubosq-Brasil-Bouin reagent for 5 minutes at 60°C. or 5 minutes in 10 per cent. boiling formol-saline.

By the authors' method the characteristic inclusions—Negri bodies—which are greyish-green, sharply defined and sometimes showing an internal structure, are visible in the cytoplasm of certain nerve cells. The identification of these diagnostic features of rabies is very simple, even to the untrained eye.

The speed of diagnosis by the simple phase contrast method allows of anti-rabies treatment being instituted with the shortest possible delay.

H. J. O'D. Burke-Gaffney

Depoux, R. & Merveille, P. Sur la valeur de la réaction de deviation du complement dans le diagnostic de la rage. [**On the Value of the Complement-Fixation Reaction in the Diagnosis of Rabies**] *Ann. Inst. Pasteur.* 1956, Feb., v. 90, No. 2, 182–6. [10 refs.]

In this article the authors examine the claims made by Ando *et al.* [this *Bulletin*, 1954, v. 51, 686, 1058] that the complement-fixation test provides a valuable addition to other laboratory techniques used for the specific diagnosis of rabies in animals dead of that disease, and that it possesses the advantages of rapidity in execution and of application to brain material reaching the laboratory in a state of putrefaction.

Materials employed in the authors' investigations were: antigens prepared from only fresh or glycerinated brain substance, because of the fact that, contrary to the experience of Ando *et al.*, specimens otherwise forwarded for examination proved to be without increased antigenicity

and to have acquired marked anticomplementary power; anti-rabies serum produced by hyperimmunizing rabbits, first with an inactivated, then with a live, strain of Brazzaville street virus and showing a final protection index of 3·2 log.; and complement derived from fresh guineapig serum.

From preliminary studies it emerged that antigens prepared from the brains of mice and guineapigs experimentally infected intracerebrally with the Brazzaville strain of street virus invariably fixed complement in the presence of homologous hyperimmune serum. In the main experiment, however, in which antigens were prepared from the brains of 40 animals of various species dead of suspected rabies, the results of complement-fixation reactions were not always in harmony with those obtained when the same brains were subjected to histological examination and biological (mouse inoculation) tests. Thus while in 31 cases the results obtained with all three diagnostic methods were in complete agreement (17 positive and 14 negative), in 9 there was disagreement, the complement-fixation reaction being positive when the other tests were negative. In the case of animals infected in nature with street virus rabies the results of serological tests were, therefore, not always to be depended on.

The authors conclude that when the complement-fixation reaction is negative, the case is not one of rabies; if it is rabies, the reaction is positive. But if the reaction is positive, rabies is present in two-thirds of the cases and absent in one-third. The specificity of the reaction is, therefore, open to question. Only negative reactions should, apparently, be taken into account. *G. Stuart*

Steele, J. H. Problemas de la lucha contra la rabia. [**Rabies Control Problems**] *Bol. Oficina Sanitaria Panamericana.* 1955, Nov., v. 39, No. 5, 469–77. [17 refs.] English summary.

A general review and discussion.

Constantinescu, N., Duca, M., Duca, E. & Cheptea, A. Turbarea paralitică experimentală vindecată sau autosterilizată la animale parţial imunizate. [**Cured and Autosterilizing Rabies in Partially Immunized Animals**] *Studii şi Cercetări Inframicrobiol., Microbiol. şi Parazitol.* 1955, Jan.–June, v. 6, Nos. 1/2, 9–16. [14 refs.] French summary.

Nine mice were inoculated intracerebrally with 100 LD50 of fixed rabies virus, and each received 1 cc. of rabies vaccine of Fermi type intradermally every day until the onset of symptoms. Eight animals died of rabies encephalitis after 5–6 days, but the remaining mouse did not develop symptoms until the 10th day and suffered a modified form of infection with complete recovery after 3 weeks. Thirty mice received

7 daily intraperitoneal injections of vaccine and a challenge dose of 5,000 LD50 of fixed virus was given intracerebrally 10 days after the end of vaccination. After the onset of paralysis glucose-saline was injected subcutaneously in order to prolong the period of survival, and in 4 mice treated in this manner the brain was found to be free of virus after death. *D. J. Bauer*

PLAGUE

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, rodent hosts, transmission, pathology, diagnosis, clinical findings, treatment, control.

Goodner, K. **Toxic End Products from** *Pasteurella pestis.* **II. Toxin Yields as influenced by Conditions of Growth.** *J. Infect. Dis.* 1955, Nov.–Dec., v. 97, No. 3, 246–50.

From the experiments described the author concludes that " suppression of vegetative multiplication of an avirulent strain of *Pasteurella pestis*, whether by temperature of incubation, adverse culture media, or gaseous environment, provided bacterial cells with enormously enhanced toxigenic properties ".

Some of the examples described in support of this conclusion are as follows. When cultures were grown at 42°C. the number of cells produced was much smaller than at 26°C., which is the optimum temperature for multiplication. On the other hand the toxicity of a given number of cells grown at 42°C. was 62 times greater than for the same number grown at 26°C. Cultures grown for 48 hours at 30°C. and then for 24 hours at 41°C. gave a larger crop of cells and at the same time their toxicity was high.

Profuse growth occurred in cultures grown in Roux bottles charged with pure nitrogen. Oxygen had a slight suppressive effect and carbon dioxide was distinctly inhibitory to cell multiplication. The cells grown under nitrogen gave poor yields of toxin while cells grown under carbon dioxide had relatively high toxicity.

Numerous experiments were made to find the effects of different culture media on the toxicity of the cells. The general conclusion reached was that media favourable to cell multiplication often gave bacteria of low toxicity and *vice versa*.

The suppression of growth in the above ways which was associated with increased toxicity of the individual cells of an avirulent strain was regarded as being of special interest in connexion with the study of pneumonic plague by McCrumb *et al.* [this *Bulletin*, 1953, v. 50, 933] in 1953 in which a series of 13 cases failed to yield blood cultures and in

several cases the pulmonary involvement was not great. In spite of the absence of evidence of overwhelming bacterial multiplication the patients had high temperatures and were profoundly ill so that it seemed not improbable that there was a temperature suppression of bacterial multiplication accompanied by an enormous exaggeration of the toxigenic potential of the cells.

The present experiments have shown that an avirulent strain (EV 76) may have wide differences in toxigenicity depending on factors, known and unknown. For example, the lysate toxin levels for a given number of cells have ranged from 0·2 to 134 units per 109 cells, so that it would seem hazardous to relate toxin potential to virulence.

John W. D. Megaw

Burrows, T. W. **An Antigen determining Virulence in** *Pasteurella pestis.* [Correspondence.] *Nature.* 1956, Mar. 3, v. 177, 426–7, 1 fig.

The author suggests that the evidence presented in this paper shows that a major determinant of virulence in *Pasteurella pestis* is the antigen which confers on the organism the property of resistance to phagocytosis. This property was found to be possessed in quantity by all fully virulent strains examined and to be undetectable in the majority of avirulent strains. This antigen is regarded as the long-sought *Vi*-antigen.

Employing the agar diffusion technique the author produced visual evidence of the existence of an antigen differentiating strains sensitive to phagocytosis by the polymorphonuclear leucocytes of the mouse, from strains resistant to phagocytosis.

Virulent *P. pestis* grown on nutrient agar at 28°C. are highly sensitive to phagocytosis (V/S), but when grown for 3 hours with gentle rotation at 37°C. in tryptic-digest meat broth at *p*H 7·0 they become resistant to phagocytosis (V/R). Avirulent organisms grown at 28°C. are also highly sensitive (AV/S) and remain sensitive at 37°C. (AV/" R ").

Antisera prepared in rabbits against V/R when added *in vitro* to V/R organisms can render them sensitive to phagocytosis. In the same conditions antisera against AV " R " are poorly able to render V/R sensitive. Both the above antisera contain many antibodies in common; they differ very little in their content of the antibody to fraction I, though this is the antibody which is regarded by many workers as playing the chief part in protecting against virulent infection, fraction I itself being regarded by some experts as being associated with virulence. The author does not agree with these views. He has found the V/R strains to have a low content of fraction I, to have no visible capsule, and to be poorly agglutinated by high-titre rabbit antiserum prepared against purified fraction I. This antiserum does not render V/R sensitive to phagocytosis. For these reasons it is considered that some antigen other than fraction I is responsible for resistance to phagocytosis, and therefore for

virulence. A photograph shows how the agar diffusion test clearly differentiates the strains sensitive to phagocytosis from those that are resistant. *John W. D. Megaw*

CHOLERA

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

Pollitzer, R. **Cholera Studies. 6. Pathology.** *Bull. World Health Organization.* Geneva. 1955, v. 13, No. 6, 1075–1199. [Numerous refs.]

This sixth section of the Cholera Studies [this *Bulletin*, 1956, v. 53, 315] deals with the pathology of the disease. The first part includes (a) the results of investigations on the experimental infection of mammals by various routes, (b) pathogenicity for lower animals, and (c) observations on the vibrio in insects. The second part deals with (a) the morbid anatomy of cholera in man, (b) the distribution of the vibrio in the tissues, and (c) pathogenesis.

Pathogenesis for mammals. An account of the studies on experimental infections which have been made is presented at considerable length and covers almost all published material from the time of Koch's discovery of the vibrio. Much of it is mainly of historical interest.

Infection by the oral route. Koch failed to infect white mice and other experimental animals by feeding with cholera faeces or cultures without special preparation although he was able to produce a fatal infection by intraperitoneal injection of large doses of culture. He was, however, able to produce a fatal infection by introducing a culture into the stomach of the guineapig after preliminary alkalinization of the stomach contents and intraperitoneal injection of tincture of opium. In animals so infected the stomach and intestinal tract were found to be distended by colourless flocculent fluid which was almost a pure culture of *V. cholerae*. A similar result was sometimes obtained when a non-cholera vibrio strain was used. Sobernheim found suspensions of heat killed vibrios administered under the same conditions to produce a similar effect. This was taken to indicate that the factor concerned was an " intoxication ". Other workers employed Koch's method, or variations of it, with success, on intestinal infection without any tendency to general invasion of the tissues following oral administration of the culture. Burrows, however, found that when guineapigs were submitted to X-radiation and similarly treated a generalized bacterial infection was produced. One method found successful in producing intestinal infection consisted in reducing

the normal intestinal flora by preliminary starvation of the experimental animal and administration of streptomycin. Details are given of corresponding investigations on oral infection of rabbits, monkeys, sisels, mice, dogs and cats by a variety of methods which were successful in varying degree.

Subcutaneous infection. The subcutaneous injection of a considerable dose of a toxigenic strain of *V. cholerae* in guineapigs and some other experimental animals has been found to produce a fatal infection. A generalized infection with bacteraemia occurs with a suitable dose but the vibrio is not as a rule present in the small intestine in the large numbers seen after successful oral infection. The same result may be produced by some non-cholera strains.

Intraperitoneal infection. By this route a suitable dose will produce a generalized infection with death from toxaemia. The findings of different workers on the presence of the vibrio in the intestine seem to have varied.

Intravenous infection. The results vary with the dose of culture given, the age of the experimental animal and other factors. If the dose is a heavy one, death from toxaemia may take place in a few hours; with a lesser dose a generalized septicaemia develops. A portal septicaemia has been noted to occur with the appearance of the vibrio in the intestine. Ray has postulated an enterotropism of the cholera vibrio which results in its becoming established in the intestine when reaching it through the blood stream. In discussing the results of parenteral cholera infection it is commented by the author that " While some felt convinced that only intoxication resulted, others thought that a generalization of the infection occurred or even held that after a passing phase of bacteraemia parenteral cholera inoculation led in an obligatory manner to a purely enteric affection ".

Action of cholera toxin.—As shown above heat-killed cultures of *V. cholerae* administered in the same way as living cultures have been found to produce similar effects, the action being that of cholera endotoxin. In contrast Chamberland-filtrates were shown to have no lethal action : an account is given of further experiments with the endotoxin, and with endotoxin fractions including nucleo-proleid, certain of the fractions being found to give a rapid fatal effect on intravenous injection in very small dosage and somewhat more slowly after intraperitoneal injection. The susceptibility of different animal species was found to vary. When death was delayed beyond 24 hours desquamation of the intestinal epithelium with congestion of the capillaries of the mucosa was sometimes noticed to have occurred. Alterations were also found in the kidneys including hyaline changes in the glomeruli and sometimes oedema and haemorrhages. Parenchymatous hepatitis and congestion of the suprarenals were also produced. On intraperitoneal injection of rabbits with heat-killed suspensions of the vibrio, there was an outpouring of fluid

into the peritoneal cavity and, in consequence haemoconcentration and a fall of blood pressure partly due to haemoconcentration and partly to the toxic action on the cardiovascular system. De and his colleagues who noted these conditions pointed out the importance of the increased permeability of the capillaries produced by the action of the toxin in the intestinal mucosa and to its effect in producing oedema of the myocardium. They had also noted its effect on the vasculature and parenchyma of the kidney which resulted in a diversion of the toxin-laden blood from the cortex to the medulla thus protecting the cortical elements from further damage. The glomeruli are rendered ischaemic, filtration of urine is lessened and the further loss of fluid diminished. When the toxin dose is very heavy the protective mechanism fails. Tests carried out on isolated organs have further demonstrated the toxicity for capillary endothelium and the increased permeability of living membranes submitted to the action of the endotoxin.

Pathogenicity for lower animals. An account is given of results of experimental infection of pigeons, chick embryos, frogs, lizards, etc. The interesting points in this section are those relating to the presence of the vibrio in fish and shellfish—it having sometimes been suggested that its survival for some period or even multiplication in such foodstuffs may be a source of infection for man. Some of the earlier observations on the subject, may be unreliable owing to failure in accurate identification of *V. cholerae* but there appears to be some reliable experimental evidence that the vibrio may survive in the bodies of fish and shellfish for some days without multiplication.

Observations on insects. The possibility that some insects, particularly house-flies may carry infection has frequently been considered and there is evidence that they may do so for short periods. The vibrio has frequently been isolated from the body surface of flies and from their internal organs. Some workers have claimed to have isolated the vibrio for periods up to 5 days but others failed to do so for longer than 24 hours. It seems unlikely that flies serve as reservoirs of infection for prolonged periods.

Pathology of human cholera. A very full account is given of the morbid anatomy of the disease in man based on the numerous studies which have been made on the general post-mortem signs and on the conditions observed in the tissues and organs, each of which is dealt with. It is recognized that the findings will vary with the period which has elapsed between the onset of the attack and death, the amount of intravenous transfusion given and the period elapsing between death and the performance of the post-mortem examination. The conditions found in the intestines and kidneys are dealt with at considerable length. This section does not lend itself to abstraction but will form a useful source of reference.

Distribution of the vibrio in the body. In patients dying within 7 days

of onset the vibrio is found in the intestinal lumen and may be found later in some cases. It is also present on the surface of the mucosa and between the epithelium and the basal membrane and in Lieberkühns crypts. Its presence deeper in the mucosa seems doubtful. It is sometimes present in the stomach, especially when vomiting has occurred. The vibrio is frequently present in the gall bladder and biliary passages and tends to persist there. Invasion of the mesenteric lymph nodes is frequent and CHATTERJEE found it in 25 per cent. of his autopsies. In a series of cases examined by GREIG he found it also in the liver, spleen, lungs and kidneys in small numbers. Cultural examinations of the blood made by many workers appear usually to have given negative results. Cultures of the urine made with due precautions appear also to have been negative. The results of the blood and urine examinations suggest that a pre-agonal generalization of the infection is exceptional.

Pathogenesis. As the result of his early investigations KOCH, in 1884, maintained that the signs and course of cholera could be explained on the assumption that the comma bacilli produced a specific poison. "The symptom complex of the cholera attack proper, usually considered to be due to dehydration and a concentration of the blood, is in my opinion to be considered essentially as an intoxication." Koch's view was supported by others at the time and it was pointed out that the damage to the intestinal epithelium would readily permit of the absorption of the toxin. The appearance of immune bodies in the serum of survivors from the attack was taken as evidence of the absorption. Other workers later recognized the importance of the loss of body fluid attributable to the action of the endotoxin in increasing the permeability of the capillaries of the intestinal mucosa. The relative importance of fluid loss and toxaemia has been the subject of controversy. It is commented that "it would be unwise to assume that the cholera toxin exerts exclusively a local action on the intestinal tract. There can be no doubt that an absorption of the toxin does take place and it is most likely that some of the lesions becoming manifest in the course of cholera outside the gastro-intestinal tract, for instance the degeneration of the striated muscles, observed also in other infectious diseases, are due to its direct action. . . . "Hence, overshadowed as it is by the spectacular manifestations due to dehydration and its sequelae, a direct role of the toxin in the causation of the general cholera syndrome should not and cannot be disregarded." *J. Taylor.*

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

Rees, C. W., **Problems in Amoebiasis.**

This book was reviewed on p. 517.

Greenberg, J., Taylor, D. Jane & Bond, H. W. **Simple Aliphatic Substrates in the Culture of** *Entamoeba histolytica*. *Amer. J. Trop. Med. & Hyg.* 1955, Nov., v. 4, No. 6, 1002–5.

The authors have devised a simple medium for the cultivation of *Entamoeba histolytica* with a mixed bacterial flora, and describe the effect upon the growth of the amoebae of the addition of 33 different compounds.

The basic medium consists of the following salts and albumin (amounts in mgm. per litre); NaCl, 8,000; KH_2PO_4, 450; $CaCl_2.4H_2O$, 250; $NaHCO_3$, 200; $MnSO_4.4H_2O$, 1·25; $ZnSO_4.7H_2O$, 0·125; $CuSO_4.5H_2O$, 3; $Fe_2(SO_4)_3$ + aq., 1·25; egg albumin, 2,500. The test substances were added in the proportion of 250 mgm. per 75 ml. of the basic medium, then brought up to 100 ml., with *p*H 7·1–7·5. The final medium was distributed in test-tubes in amounts of 5 ml., and autoclaved, after which rice powder was added. Each tube was inoculated with 0·5 ml. of the pooled sediment of 24-hour cultures of *E. histolytica*.

The results were assessed on the basis of the length of maintenance of a culture under given conditions. It was shown that in all the experiments but one, successful cultures were obtained with added aliphatic amines, comprising primary, secondary, and tertiary amines, in which the number of carbon atoms varied from 1 to 6, as well as mono- and polyhydroxy amines. The cultures were unsuccessful with added non-amino compounds (with one exception), comprising carboxylic acids, alcohols, hydroxyamino acids. The exception was fumaric acid, which promoted growth of the amoebae.

It is suggested that the amines might play the following roles in the cultures: (a) act as a buffer as well as source of C and N, (b) yield a common metabolite required by the amoebae, or (c) support the growth of a limited number of concomitant bacteria best suited for the growth of the amoebae. *C. A. Hoare*

Floriani, C., Cellerino, N. A. & Cellerino, R. J. Diagnóstico práctico de la amebiasis intestinal. (Nuevo método de coloración.) [**Practical Diagnosis of Intestinal Amoebiasis (New Staining Method)**] *Semana Med.* 1955, Dec. 15, v. 107, No. 24, 1178–80.

A description is given of a new staining method for the differential diagnosis of human intestinal amoebae.

Moist faecal smears, spread on coverslips, are fixed for 10–15 minutes in Schaudinn's fluid containing 5 per cent. acetic acid, after which the preparations are washed for 2–3 minutes in 70 per cent. alcohol containing iodine, and then washed twice (2–3 minutes each time) in distilled water. They are then stained for 2–5 minutes in 0·5 per cent. aqueous solution of toluidine blue, after which they are passed through 3 changes of absolute alcohol, thence into xylol, and mounted in Canada balsam.

The nuclei of the amoebae stain blue, while the cytoplasm is tinted grey. Since the parasites are adequately stained without differentiation, this method can be entrusted to laboratory technicians. Its only disadvantage is that the preparations tend to fade after 2 months.

C. A. Hoare

Brown, C. H., Gebhart, W. F. & Reich, A. **Intestinal Amebiasis. Incidence, Symptoms, and Treatment with Arsthinol (Balarsen).** *J. Amer. Med. Ass.* 1956, Feb. 4, v. 160, No. 5, 360–63. [Refs. in footnotes.]

Some 2 per cent. of 7,826 stools examined in Cleveland Clinic Foundation between 1950 and 1952 were found to contain *Entamoeba histolytica.* The presence of the parasite in 75 patients was coincidental with, and not the primary factor in the causation of, the patients' complaints. Thirty-four patients were treated with 5 " tablets " of Arsthinol (Balarsen) [this *Bulletin*, 1955, v. 52, 45] daily for 5 to 7 days; 3 suffered side-effects in the form of diarrhoea and colic. In 31 of the 34 a parasitic diagnosis was established; in the other 3 it was inferential on proctoscopic examination though negative on microscopic. Re-examination of the stools of those treated, between 1 and 15 months later, failed to yield parasites; only 54 stools were examined from the 31 patients originally parasitically positive. The rectal changes seen in the other 3 had cleared after the Arsthinol treatment.

A. R. D. Adams

Mentasti, G. & Grassi, L. Su 25 casi di amebiasi intestinale curati con fumagillina. [**On 25 cases of Amoebiasis cured with Fumagillin**] *Giorn. di Malattie Infettive e Parassit.* Rome. 1956, Jan., v. 8, No. 1, 30–32.

The authors treated 25 cases of amoebiasis among the nursing staff of the Ospedale Maggiore of Milan, and were able to follow them up for a year. Fumagillin was selected as the authors have not had absolutely satisfactory results with emetine, aureomycin, oxytetracycline or with arsenical or quinoline compounds.

Of the 25 patients who were asymptomatic or practically so, 20 had vegetative, and 5 cystic forms of *E. histolytica* in the stools; 5 patients

had already been treated with emetine and Stovarsol, or aureomycin and Stovarsol, and had relapsed; 2 had had an acute attack of dysentery with characteristic faeces shortly before. In view of the literature the authors decided to use a dosage of 40–60 mgm. of fumagillin (Fumidil Abbott) per day for 10 days. Almost all the patients complained of some disturbance during treatment, probably owing to the high dosage, but it was not necessary to stop it in any case. Eight patients had a maculo-papular rash on the fingers and toes, with subsequent desquamation, and 12 had colicky abdominal pain. One patient had a more serious illness, with a similar maculo-papular eruption on the face and breast as well as on the extremities, passage of pultaceous or semi-liquid stools, anorexia, and asthenia, and the dosage was reduced to 20 mgm. per day for 15 days. Antihistamine and liver-protecting drugs were also given. Examination of urine, blood films, blood urea, blood sugar and of liver function carried out before, during, and after treatment showed no appreciable difference. There was no leucopenia—which the authors consider an important point. Monthly examinations of the stools were made, and all the patients remained negative to *E. histolytica* after 10 months.

The authors admit that they did not know whether intestinal ulceration was present, as the result of the recto-sigmoidoscopic examinations was " lacking ". However, they feel that as their cure rate is 100 per cent. it is essential to test the drug on a large number of patients.

W. K. Dunscombe

Rodriguez, C. & Adrianza, M. Complicaciones pleuropulmonares de la amibiasis. [**Pleuropulmonary Complications in Amoebiasis**] *Rev. Sanidad y Asistencia Social.* Caracas. 1953, Jan.–Apr., v. 18, Nos. 1/2, 117–45. [16 refs.]

The English summary appended to the paper is as follows:—

" Ten cases of pleural and pulmonary complications of amebiasis are presented, these were found among a total of one thousand clinical cases of the Thoracic Service at the Instituto Oncológico ' Luis Razetti ' in Caracas, studied during the last two years.

" An increase in the incidence of these complications in the last two years is noted. This increase is interpreted as being due possibly to the limited use of Emetine in the treatment of the acute phase of intestinal amebiasis as well as the almost total histories reviewed. There is a greater incidence among men; the disuse of a therapeutic test with this drug in hepatitis with a previous history of intestinal amebiasis.

" The cases reported represent 1% of the total number studied. There were more cases in males, the proportion to females being 10 to 1.

" The pathogenesis of the various pleuro-pulmonary complications of amebiasis is reviewed. These lesions are brought about by the vegetative forms which gain access to the thoracic organs through veins or lymphatics in the vicinity of the ' collar button ' ulcers in the colon. A classification

of the lesions is proposed into pleural and pulmonary. Each is analyzed individually with reference to the clinical picture symptoms, radiological and laboratory findings and treatment."

Gordon, G., Wilmot, A. J. & Elsdon-Dew, R. **Camoquin in Amoebic Liver Abscess.** *J. Trop. Med. & Hyg.* 1955, June, v. 58, No. 6, 133–5.

Five African males with uncomplicated amoebic liver abscesses, from which "characteristic pus" had been aspirated, were treated with Camoquin [amodiaquine]. The dose was 600 mgm. daily by mouth in two 10-day courses, with an interval of 8 to 10 days. Diiodohydroxyquinoline was given concurrently to those patients [apparently one] who also had dysenteric symptoms. The relevant clinical and laboratory data are set out in a table; from this it will be seen that the immediate response in 3 cases was good, and in the other 2 less satisfactory though not bad. No toxic side-effects attended the use of the drug. In the authors' view emetine hydrochloride remains the drug of choice for the treatment of amoebiasis of the liver; chloroquine is of great value; and amodiaquine is also effective. *A. R. D. Adams*

Shaffer, J. G. & Ansfield, J. **The Effect of Rabbit Antisera on the Ability of *Entamoeba histolytica* to Phagocytose Red Blood Cells.** *Amer. J. Trop. Med. & Hyg.* 1956, Jan., v. 5, No. 1, 53–61.

The uncertain results of serological tests for the diagnosis of amoebiasis might be due to the existence in *Entamoeba histolytica* of strains varying in antigenic constitution. Since no exact data regarding such variation are available, the authors sought to throw light on this phenomenon by studying the inhibitory effect of anti-*histolytica* rabbit serum on the ability of these amoebae to ingest erythrocytes.

Cultures of 7 strains of *E. histolytica* were repeatedly inoculated into rabbits to produce antisera, and 3 samples of serum were collected from each rabbit—before inoculation (normal), 7–10 days after, and after a later "booster" inoculation of amoebae. In the experiments, serum from each rabbit was tested against all the strains of *E. histolytica*. For this purpose, in 48-hour rich cultures most of the covering fluid was removed, leaving 1·75 ml.; 0·25 ml. of the serum was added to each tube, then the tubes were kept for 2 hours at 37°C. On removal from the incubator, 0·3 ml. of 1 in 10 dilution of defibrinated rabbit blood was added, and the tube was replaced in the incubator for 15 minutes, after which the unphagocyted erythrocytes [RBC's] were haemolysed by addition to each tube of 10 ml. distilled water. Finally, the results were read by taking a sample from the tube between slide and coverslip, counting the number of RBC's in each of the first 25 amoebae and calculating the average, which represented the phagocytic index.

These experiments provided information both on the inhibition of phagocytosis by antisera and on variation in the power to phagocytose RBC's exhibited by different strains of *E. histolytica*. It was shown that each strain had a definite and constant range of phagocytic activity, characterized by a normal curve, the peak of which corresponded to the phagocytic index, which had the following values for the strains tested: 12·7, 12·5, 10·5, 8·3, 7·6, 7·1, 4·5. The tests on inhibition of phagocytosis by rabbit sera showed that homologous anti-amoebic serum produced a marked reduction in the phagocytic index (72–85 per cent.), compared with normal serum, while the effect in the case of heterologous systems, though present, was less pronounced. On comparing the behaviour of all the strains in these tests, it was found that some showed cross-reactions, indicating closer relations between certain strains, whereas one appeared to be distinct from all the others.

In discussing these experiments, " It is suggested that these results indicate antigenic variation among strains of *E. histolytica* ".

C. A. Hoare

Swerdlow, M. A. & Burrows, R. B. *Dientamoeba fragilis*, **an Intestinal Pathogen.** *J. Amer. Med. Ass.* 1955, May 21, v. 158, No. 3, 176–8, 2 figs.

Pursuing their original observations [this *Bulletin*, 1955, v. 52, 371] the authors have sectioned vermiform appendices removed at U.S. Army and Air Force hospitals, and fixed in 10 per cent. formaldehyde. *Dientamoeba fragilis* was found in 15 (1·3 per cent.) of 1,130 appendices examined—this is about twice the incidence of the parasite in routine stool specimens examined in the laboratory during the same period. Only 3 of these appendices had *D. fragilis* as the sole parasitic content; the others also contained *Chilomastix mesnili*, *Entamoeba coli*, *Giardia intestinalis*, *Strongyloides stercoralis*, *Enterobius vermicularis* or *Trichuris trichiura*. In all cases of infection some of the *D. fragilis* were seen to contain red cells but, as previously, no evidence of tissue penetration was forthcoming. The appendicular changes ranged from acute suppurative appendicitis to lymphoid hyperplasia of the appendix, but fibrosis was evident in all of them. Of 18 appendices containing solely *Enterobius vermicularis* only 4 (22·2 per cent.) showed fibrosis; of 11 containing *E. coli* only one was fibrotic; of 7 with *G. intestinalis* one showed fibrosis; and others with parasites other than *D. fragilis* equally showed only occasional evidence of fibrotic change. The fibrosis occurred equally among all age-groups, and in the authors' opinion was directly due to the action of the *D. fragilis* infection as a low-grade irritant over a period. *D. fragilis* infections therefore should be eradicated whenever encountered [though the method is not stated]. *A. R. D. Adams*

RELAPSING FEVER AND OTHER SPIROCHAETOSES

Hara, J. **Some Notes on the Habits of the Tick,** ***Ornithodoros tholozani*** **Laboulbene and Mégnin (***O. papillepes* **Birula).** *Japanese J. Exper. Med.* 1955, Apr., v. 25, No. 2, 65–8, 1 fig. on pl.

"The author has been rearing and observing the soft tick, *Ornithodoros tholozani*, since 27 April, 1952. Remarkable habits noticed during observations are as follows:—

"1. The intervals of successive feedings are not constant, the shortest interval being 8 days and the longest more than two months.

"2. The ticks seem to molt after full engorgement. Those which fail to molt invariably die.

"3. They engorge immediately, or at least within three weeks, after the molt.

"4. The shortest period from molt to molt is 7 days.

"5. One female laid 135 eggs in 6 batches during 17 days.

"6. The shortest length of egg stage is 14 days and the longest 23 days, most of them hatch within 18 to 21 days.

"7. Mortality is high, i.e., 32·1 per cent.

"8. The larvae can engorge human blood, with some precautions, and feedings are done at least every 4 days."

ERRATUM

The author of the paper on **Relapsing Fever in the Digo District of Kenya Colony,** abstracted in this *Bulletin*, 1956, v. 53, 449, has written to point out that in the *East African Medical Journal* the area referred to was erroneously stated to be of some 8 square miles. This should have been 80 square miles. The figure 8 in the eleventh line of the abstract should therefore be altered to 80.

YAWS AND OTHER TREPONEMATOSES

Montel, M. L. R. Chancres pianiques persistants. Essai d'interprétation biologique. [**Biological Observations on Persistent Yaws Lesions**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 3, 346–9, 2 figs. on 2 pls.

The author discusses the tissue changes which occur in persistent lesions of primary yaws. He comments on cases illustrated in a previous

publication (Montel, *Semaine des Hôpit. de Paris*, 1951, v. 27, 453). In one man of 60 years of age a primary yaw persisted for 2 years. The author discusses the hypertrophy of tissue which leads to a chancre-like primary lesion of yaws continuing after a florid secondary eruption has appeared. Primary yaws may also take the form of a large tropical ulcer which yields rapidly to specific treatment. A persistent primary yaw may become modified in structure or heal with the onset of a generalized secondary eruption suggesting that a change in immune response is occurring. If the primary yaw is unaffected by the eruption it will tend to heal at the time of resolution of the secondary eruption. [The local tissue response in yaws is certainly remarkable and worth further study.]

Frederick J. Wright

LEPROSY

In this section abstracts are arranged as far as possible in the following order:—epidemiology, aetiology, pathology, diagnosis, clinical findings, treatment, control.

Convit, J. & Gonzalez, C. L. Aspectos epidemiológicos de la lepra en Venezuela. [**Epidemiological Aspects of Leprosy in Venezuela**] *Rev. Sanidad y Asistencia Social.* Caracas. 1954, Sept.–Dec., v. 19, Nos. 5/6, 373–86, 3 charts on 3 pls.

The English summary appended to the paper is as follows:—

" The foregoing is the history of the creation and organization of the Leprosy Division, Ministry of Health and Social Welfare.

" The magnitude of the work carried out by the leprosy control services of the Division is emphasized. In 76 Municipalities of the States of Tachira, Trujillo, Merida, Miranda and Aragua 293,954 persons were examined, 224,306 of them belonging to the rural areas.

" A description of the leprosy control services and of the way of making the leprosy surveys is given.

" The authors present some of the epidemiological characteristics of leprosy in Venezuela. It is noted that by the end of 1950 there were 5,550 known cases, of which 1,573 isolated in the national leprosaria and 4,017 cases under treatment and control by local dispensaries.

" The case-type percentage among the known cases is 58·4 for lepromatous, 21·4 for indeterminate and 20·2 for tuberculoid types.

" The fact is presented that in the Andean states (Merida, Tachira and Trujillo) the types of leprosy among non-isolated cases were found in approximately the same proportion (around 1/3 for each type) while in the State of Miranda the proportion of the lepromatous type was hardly 10%. Without going into definite interpretations the authors

believe that these epidemiological characteristics are due to racial factors."

Chaussinand, R., Viette, M. & Prudhomme, R. O. Note préliminaire sur la préparation d'une lépromine standardisée. [**Preliminary Note on the Preparation of a Standardized Lepromin**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 6, 784–8.

The objection to the lepromin antigen prepared according to Wade's method by filtration through nylon is that an amount of tissue debris remains, and that the bacilli are gathered together in masses or globi. This massing of bacilli is an even greater disadvantage when it is sought to dilute the antigen, both as a measure of economy and in order to test the degree of sensitivity to the antigen. Grinding up with glass powder is not suitable, as this does not dissociate the masses sufficiently and fine particles of glass are left in the suspension. Two methods have been found to give promising results.

(1) Treatment of Wade's antigen with 1 per cent. papain, raising the temperature to 70° during 5 minutes, keeping it at 70° for 5 minutes, and then boiling for 5 minutes. It was found that when this was filtered through nylon, about one-third of the tissue debris had been eliminated.

(2) Ultra-sonic action was used to dissociate the bacilli in a suspension of Stéfansky's bacillus. With a frequency of 960 kilohertz and 90 watts applied for 15 minutes there was a diminution in the number and size of the masses. In 3½ hours the majority of the masses were dispersed, though a few small ones persisted, but the number of the bacilli seemed to have diminished.

By a similar method with a lepra bacillary suspension applied for 4 hours, and examination of a drop of the suspension every 15 minutes, it was found that after 30 minutes the number of globi had diminished but the number of single bacilli was the same. By 45 minutes the bacilli had diminished by half. By 4 hours there were very few masses and globi, and very few isolated bacilli. *Myco. leprae* had thus much less resistance to supra-sonic vibrations than Stéfansky's bacilli.

Using this 4-hour treated suspension of lepra bacilli to test patients, the authors found the early reaction slightly stronger than with the ordinary antigen, and the delayed reaction practically identical with it. However, in lepromatous patients a slight local reaction was noted which lasted for a few weeks and attempts were made to find out if this was due to the partly broken up tissue debris or to the supra-sonic treatment of the bacilli. It was found that the injection of the supranatant fluid after centrifuging the treated antigen for half an hour, produced no local reaction in allergic patients. It was found that the papain-treated antigen does not give any false positive reactions, but is rich in bacilli. It is hoped by combining the two methods to produce a reasonably homogeneous antigen suitable for dilution. *Ernest Muir*

Baldo, J. I. Investigación de la Tuberculosis en medio leproso. [**Investigation of Tuberculosis in Those Suffering from Leprosy**] *Rev. Sanidad y Asistencia Social.* Caracas. 1954, Sept.–Dec., v. 19, Nos. 5/6, 361–71.

The investigation was made in the patients of the Cabo Blanco Leprosarium, Venezuela. The patients had been examined for tuberculosis 12 years previously and were now re-examined. Tuberculin allergy showed a high positivity in 709 leprous patients, with an early incidence in the younger groups comparable with that found in those with poor economic and social standards outside the leprosarium. The positive percentage was rather lower in the second than in the former enquiry, but this could be accounted for by a difference in the Mantoux technique.

Chest photography in 827 leprous patients, first with microfilms, and then with 30 × 40 cm. films in those with abnormal appearances, followed by examination of sputum of those suspected of suffering from pulmonary tuberculosis, gave 10·7 per cent. of pathological findings, compared with 21·2 per cent. in the former examination. Those with early active tuberculosis were only 0·6 per cent. compared with 3·2 per cent. formerly; and those with more advanced disease only 2·0 per cent. compared with 6·7 formerly.

There is thus a marked decline in the incidence of tuberculosis. This may be due partly to better hospital conditions, but the chief reason for the improvement is probably the effects of sulphone therapy, which improves the general health of the patients. The atypical trabecular and reticular shadows due to leprosy of the respiratory passages are also much less. *Ernest Muir*

Merklen, F. P. & Riou, M. V. Survenue d'une tuberculose pleuro-pulmonaire dans une lèpre lépromateuse au cours du traitement cortisonique d'une réaction lépreuse. [**Development of Pleuro-Pulmonary Tuberculosis in a Patient with Lepromatous Leprosy during Treatment with Cortisone for Lepra Reaction**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 6, 778–82.

Floch, H. La lèpre favorise-t-elle l'apparition de la gale norvégienne? [**Does Leprosy Favour the Appearance of Norwegian Scabies?**] *Bull. Soc. Path. Exot.* 1955, v. 48, No. 6, 796–800.

Two patients are described suffering from this condition, one of them also suffering from advanced tuberculoid leprosy. The opinion that this form of skin disease is favoured by the anaesthesia of leprosy is refuted by the statement of Orsini that it is found most frequently in the lepromatous type of leprosy in which anaesthesia is less marked than in the

other types. The condition was first described by DANIELSEN and BOECK, the Norwegian dermatologists, and hence the name used.

In the two cases described there was extensive encrustation of the skin, and the diagnosis was made by finding large numbers of *Sarcoptes scabiei*. The 3 clinical characteristics of the condition are: horny formations, polymorphic eruptive elements and erythrodermia. The question asked in the title is left unanswered as the first patient had lived for 25 years in Guiana, where leprosy is so common, without becoming affected with leprosy, and the second patient had marked anaesthesia of the limbs.

Ernest Muir

See also p. 947, BROWN, **Observations on the General Incidence of Blindness and certain other Diseases in Uganda.**

HELMINTHIASIS

*In this section abstracts are arranged as far as possible in the following order:—*TREMATODES *(schistosomes, other flukes);* CESTODES *(Diphyllobothrium, Taenia, Echinococcus, other cestodes);* NEMATODES *(Hookworms, Ascaris, Filarial worms, Dracunculus, etc., Trichuris, Enterobius, Trichinella, etc.).*

TRAPNELL, D. H. **Eosinophilia in East African and Mauritian Troops. An Analysis of 150 Cases.** *J. Roy. Army Med. Corps.* 1956, Jan., v. 102, No. 1, 73–6, 3 figs.

Among 178 consecutive cases of eosinophilia found in routine investigation of East African and Mauritian troops in the Canal Zone in Egypt, the author found a cause for the eosinophilia in 66 and 84, respectively. Eosinophilia was taken to be present if the eosinophils in the blood exceeded 250 per cmm. and the degree was assessed as minimal, mild, moderate or gross, the 4 grades ranging between 250 and 3,000 or more per cmm.

The results are shown in 2 tables and 3 figures from which it is evident that a moderate eosinophilia (1,000 to 2,999 per cmm.) was most commonly found. In all but 2 cases, intestinal parasites (sometimes multiple) were found. The incidence of the different parasites shows that hookworms were commonest: in Mauritians it was commonly associated with *Trichuris*. *Taenia* was common in East Africans and *Ascaris* in Mauritians. There were 9 cases of *Schistosoma mansoni* infection, all in East Africans: few cases of *S. haematobium* were found.

Details are given of 15 cases of helminthic infections in which no eosinophilia was found and of 20 East Africans and 8 Mauritians in whom the cause of eosinophilia could not be determined.

Among 90 cases of hookworm infection, only one man (East African) had less than 11·0 gm. of haemoglobin per cent.

Five Mauritians and 3 East Africans with acute bronchitis and eosinophilia were found, but no larvae were discovered in the sputum. One East African with eosinophilia showed X-ray features suggesting pulmonary eosinophilia. [See also Cronk, this *Bulletin*, 1956, v. 53, 205.]

H. J. O'D. Burke-Gaffney

Dinulescu, G., Stoenescu, D., Manoiu, I., Rauchbach, C., Drágoiu, I., Donciu, I. & Fruchter, J. Cercetări asupra piperazinei ca antihelmintic în ascaridoză, anchilostomoză şi trichuroza la cîine. [**Piperazine as an Anthelmintic in Ascariasis, Ankylostomiasis and Trichuriasis in Dogs**] *Studii şi Cercetări Inframicrobiol., Microbiol. şi Parazitol.* 1955, Jan.–June, v. 6, Nos. 1/2, 285–93. French summary.

Dinulescu, G., Stoenescu, D., Manoiu, I., Ilie, I., Vişan, C., Teodoru, M., Rauchbach, C., Negru, I. & Lovin, D. Piperazina ca antihelmintic în parascaridoză, oxiuroză şi strongiloză la cai. [**Piperazine as an Anthelmintic in Parascariasis, Enterobiasis and Strongyloidiasis in Horses**] *Studii şi Cercetări Inframicrobiol., Microbiol. şi Parazitol.* 1955, Jan.–June, v. 6, Nos. 1/2, 295–300. French summary.

van Beukering, J. A. & Vervoorn, J. D. **Sterility in an African. Report on a Case.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1956, Mar., v. 8, No. 1, 61–2.

"An African woman complained of sterility of three years' duration. She was found to be normal, but her husband suffered from azoospermia and bilateral hydrocele; the fluid of the latter contained ova of *S. haematobium* on the left side and an unidentified microfilaria on the right side."

Riggin, G. T., Jr. & Berrios, L. A. **The Pig as a Host of** *Schistosoma mansoni* **in Puerto Rico.** [Research Note.] *J. Parasitology.* 1956, Feb., v. 42, No. 1, 10.

In Puerto Rico pigs spend a considerable time in streams supporting colonies of *Australorbis glabratus* which have a high incidence of *Schistosoma mansoni.*

The authors obtained 2 pigs, aged 40 and 50 days, from sources where there was little likelihood of exposure to *S. mansoni.* The younger animal was then exposed once to 3,550 cercariae from 10 or more snails by immersion of the posterior half of the body for 45 to 60 minutes. The

older animal was exposed to 10,000 cercariae on 8 occasions in 3 weeks. In both cases severe irritation was present during and immediately after exposure and a local rash was usually present: this was most marked in the pig which had multiple exposures.

The faeces of the younger pig were negative for *S. mansoni* up to 68 days. The animal was then killed and 1 male and 4 female worms were found in the mesenteric veins; viable and dead eggs were found in the liver, intestinal wall and mesentery.

The faeces of the older pig were also negative. It was killed on the 83rd day: no adult worms were found, but many dead and a few living eggs were found in the liver. In all cases the eggs were heavily encapsulated.

At the abattoir at Caguas, a highly endemic area, blood, faeces and pieces of viscera are commonly flushed off the floor and drained into the river: any viable eggs present could thus hatch in the vicinity of the snail vector. Examination of 35 to 40 pieces of tissue from pigs at this abattoir failed to show *S. mansoni* eggs, so that if any were present the number was small. There was a fairly high incidence of *S. mansoni* in snails below the abattoir, but other sources of infection were present.

It would seem that *S. mansoni* can mature and produce viable eggs in the pig, but it is a poor host. It does not seem likely that the pig plays a part in transmitting *S. mansoni* infection in Puerto Rico.

H. J. O'D. Burke-Gaffney

Paraense, W. L., Pereira, O. & Pinto, D. B. Um aspecto da ecologia do *Australorbis glabratus* que favorece a reinfestação dos criadouros. [**An Ecological Feature of** *Australorbis glabratus* **favouring Re-Infection of Breeding Places**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1955, June, v. 7, No. 2, 573–81. [13 refs.]

The English summary appended to the paper is as follows:—

"During an investigation carried out in the city of Tarumirim, State of Minas Gerais, for the purpose of valuing the effectiveness of pentachlorophenol against *A. glabratus*, living snails were found buried both in the mud of the edges, and in the soil about 2 metres distant from the edges of the collections of water. These findings were made through the entire period of observation (June–December, 1954). In either case the snails were at depths varying up to 40 cm.

"The mechanisms probably involved in such behavior are discussed. We think that burrowing in the mud of the edges is connected with nutritional and/or protective habits, and that some of the snails already spontaneously buried in the mud should escape the effect of coincident treatments with molluscicides. As to the specimens buried in the soil, we admit that they reach that situation at the end of the rainy season, when after increasing, the collections of water revert to their normal

beds; then they remain isolated in temporary puddles spread over the previously inundated areas. As the latter progressively dry, the snails burrow into the soil in order to escape the resulting extreme environmental conditions. In this situation they may be found through the entire dry season, so that at the next rainy season the still living buried snails should emerge from the soil by moving through the soaked upper layers."

Bezerra, O. F. Contribuição ao conhecimento dos planorbídeos do Estado do Ceará. [**Data on the Planorbids of the State of Ceará, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, July, v. 7, No. 3, 351–5.

The English summary appended to the paper is as follows:—

"The author reports the examination of the Planorbidae of 68 localities of 15 counties of the state of Ceará (Counties of Fortaleza, Aquirás, Pacajus, Pacatuba, Redenção, Pacoti, Aracati, Aracoiaba, Caucaia, Crateús, Baturité, Granja, Maranguape, Nova Russas and Tauá) finding the following species: *Tropicorbis stramineus* (Dunker), *T. janeirensis* (Clessin), *Gyraulus melleus* (Lutz 1918), Lucena 1954, *Drepanotrema cultratus* (d'Orbigny), *D. cimex* (Moricand) and *D. anatinus* (d'Orbigny), with great predominance of the first, which, besides representing about 90 per cent of the identified specimens, was the species with the largest geographical distribution, having been found in all counties of the state. The dissection of Planorbidae of 6 counties (Redenção, Pacoti, Fortaleza, Aquirás, Pacajús and Pacatuba) showed that the only species naturally infected by *S. mansoni* was *Tropicorbis stramineus*. The examination of 5,081 specimens in the county of Redenção and 1,228 in the county of Pacoti showed the indices of natural infection of 0·25 and 0·08 per cent, respectively. In the other four counties no infected Planorbidae were found."

Martins, A. V., Martins, G. & de Brito, R. S. Reservatórios silvestres do *Schistosoma mansoni* no estado de Minas Gerais. [**Sylvatic Reservoirs of** *Schistosoma mansoni* **in Minas Gerais, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, Apr., v. 7, No. 2, 259–65. [10 refs.]

The English summary appended to the paper is as follows:—

"The authors report the results of the search for sylvatic reservoirs of *Schistosoma mansoni* in the counties of Jaboticatubas and Belo Horizonte, state of Minas Gerais. Two hundred and ten Mammifera were examined, representing 3 different orders and 17 species: *Marsupialia*—3 species and 48 individuals; *Primata*—1 species and 2 individuals; and *Rodentia*—13 species and 160 individuals. Seven species were found naturally infected, out of which 3 had already been registered as natural

reservoirs of the trematode: 1 marsupial—*Didelphis paraguayensis*, and 2 rodents—*Nectomys squamipes* and *Oryzomys subflavus*. The rest of four—*Rattus norvegicus norvegicus*, *Oryzomys mattogrossae*, *Zygodontomys lasiurus* and *Cavia aperea aperea*—all pertaining to the order *Rodentia*, are for the first time found naturally infected by *Schistosoma mansoni*. The author rapidly discusses the relative epidemiological importance of these sylvatic hosts, emphasizing the importance of the continuation of the researches. He points out that the species of trematode observed was undoubtedly *Schistosoma mansoni* Sambon, 1907, and denies, at least for the material studies by him, the acceptance of the variety *rodentorum* proposed by Schwetz."

Pablo Parilli, J. Corazón pulmonar bilharziano. Primer caso descrito en Venezuela. [**Schistosomal Cor Pulmonale; First Case in Venezuela**] *Rev. Sanidad y Asistencia Social.* Caracas. 1951, Sept.–Dec., v. 16, Nos. 5/6, 541–59, 6 figs. on 6 pls. (2 folding). [17 refs.] English summary.

de Jesus, O. A. Primeiros resultados da profilaxia planorbídea, como método de contrôle de esquistossomose mansonica, na zona das Grotas, no Estado da Bahia. [**First Results of the Control of Planorbids in the Prevention of** *S. mansoni* **Infection, in Grotas, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, July, v. 7, No. 3, 361–2.

The English summary appended to the paper is as follows:—

"The author reports the first results of the combat against Planorbidae in the region of Grotas, state of Bahia. After the failure with the use of lime against the Planorbidae, he used copper sulphate in concentration varying between 1:100,000 to 1:300,000, with very good results. He refers a reduction of 95·9 per cent, as the number of living snails fell from 7,787 before the use of copper sulphate to only 318 after the use of this chemical."

Aguirre, G. H., Silva, J. F. & Tavarfs, M. D. Sulfato de cobre como planorbicida; seu emprêgo no Setor Bahia do Serviço Nacional de Malária. [**Copper Sulphate as a Planorbicide; its Use in the Bahia Sector of the National Malaria Service of Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, Apr., v. 7, No. 2, 235–43, 2 figs.

The English summary appended to the paper is as follows:—

"The authors report the results of the use of copper sulphate as a planorbicide in the control of schistosomiasis in the state of Bahia. The drug is effective in the dosage of 1:50,000 to 1:100,000 and was applied as a 10% solution to be sprayed on the surface of the water collections.

The treatment had to be continued for 48 hours, and in certain cases for 72 hours. The difficulty of ascertaining the copper sulphate content of the water in low concentrations was solved by the use of the sodium diethyl-dithiocarbamate test. The copper sulphate method was used by the authors in the state of Bahia in 164 localities of 34 counties, causing a general reduction of 92% in the density of planorbids, figure that in some localities was as high as 100%."

Aguirre, G. H. Sugestão para um contrôle econômico da populacão planorbídea do único foco de esquistossomose mansoni, conhecido na Amazônia. [**Proposed Economic Method of Controlling Planorbids in a Focus of** *Schistosoma mansoni* **Infection in Amazonia, Brazil**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, July, v. 7, No. 3, 357–9.

The English summary appended to the paper is as follows:—

" As it was discovered that the liquid left over after the coagulation of the latex of rubber trees still contains about 2 per cent of sodium pentachlorophenate used to obtain the coagulation, and this chemical is known as the best molluscocide, the author experimented with good results the use of that waste liquid to kill the Planorbidae. He suggests and recommends the use of that liquid as a low cost method of Planorbidae control in the Amazônia."

Mayer, M. & Pifano C., F. Modalidades de la infección producida por *Schistosoma mansoni* en animales de laboratorio infectados con cercarias provenientes de un solo caracol. [**Method of Infection by** *Schistosoma mansoni* **in Laboratory Animals Infected with Cercariae from a Single Snail**] *Rev. Sanidad y Asistencia Social.* Caracas. 1951, Sept.–Dec., v. 16, Nos. 5/6, 445–59.

Batten, P. J., Jr. **The Histopathology of Swimmers' Itch. I. The Skin Lesions of** *Schistosomatium douthitti* **and** *Gigantobilharzia huronensis* **in the Unsensitized Mouse.** *Amer. J. Path.* 1956, Mar.–Apr., v. 32, No. 2, 363–77, 12 figs. on 6 pls. [11 refs.]

" The response of the unsensitized white mouse to cercariae of *Schistosomatium douthitti* and of *Gigantobilharzia huronensis* is very similar. The development of papules is caused by epithelial edema due to the cercariae which remain within the epidermis. Disappearance of the papules coincides with the extrusion of these dead cercariae in the stratum corneum.

" The earliest demonstrable tissue reaction against cercariae in the dermis and subcutaneous tissues is a local accumulation of histiocytes. These histiocytes serve to encapsulate the parasites. Somewhat later there is a generalized neutrophilic response, which becomes maximal

when the cercariae have become completely encapsulated. Phagocytosis of the parasites then ensues. Evidence of the inflammatory response was observed 3 weeks following exposure."

Lee, Wen-Hsing. **Roentgen Diagnosis of Pulmonary Paragonimiasis.** *Mem. College Med. Nat. Taiwan Univ.* 1955, Oct., v. 4, No. 1, 23–38, 30 figs. on 8 pls.

"1. Roentgen study was made on eighty cases of pulmonary paragonimiasis.

"2. Roentgen findings in these 80 cases are:

"(1) Haziness and soft pneumonic consolidation in 35 cases,

"(2) Dense pneumonic consolidation in 17 cases,

"(3) Nodules in 14 cases,

"(4) Radiolucencies within haziness, soft or dense pneumonic consolidation or nodules in 62 cases,

"(5) Prominent lung-markings and hilar shadows in 52 cases,

"(6) Pleural reaction in 32 cases, and

"(7) Spontaneous pneumothorax in 3 cases.

"3. Roentgen film study of the chest showed a combination of two or more of the above mentioned conditions in most cases.

"4. The radiolucencies within densities were found by the author to be the most suggestive and important sign for the diagnosis of pulmonary paragonimiasis.

"5. The diagnosis of pulmonary paragonimiasis should be confirmed by careful history taking, clinical signs and symptoms, and laboratory data, when suggestive findings are found by Roentgen study of the chest."

Schumacher, W. Untersuchungen über das Eindringen der Jugendformen von *Fasciola hepatica* L. in die Leber des Endwirts. [**Studies on the Penetration of the Young Forms of** *Fasciola hepatica* **in the Liver of the Host**] *Ztschr. f. Parasitenk.* 1956, v. 17, No. 4, 276–81, 5 figs. [16 refs.]

Kuźmicki, R. Badania nad skutecznością nasion dyni (*Sem. Cucurbitae*) w leczeniu zarażeń tasiemcem nieuzbrojonym. [**Investigations upon Efficiency of Pumpkin Seed** (*Sem. Cucurbitae*) **in the Treatment of** *Taenia saginata* **Infection**] *Wiadomości Parazytologiczne.* Warsaw. 1956, v. 2, No. 2, 85–92. [16 refs.]

The English summary appended to the paper is as follows:—

"In this paper are discussed investigations upon treatment of taeniarhynchosis by means of pumpkin seed and its efficiency. This by administering pumpkin seed in a single dose of 200–400 g, without other drugs, to 25 sick (first group of patients) and seed together with atabrine

(the latter in a dosage of 0·4 g) to 45 sick (second group of patients). In the first group treated with pumpkin seed alone, on 25 persons the tapeworm with scolex was expelled from 3 sick (about 12%) after one course of treatment and among 8 persons who underwent a second course of treatment also three recovered entirely (about 37·5 per cent). In the second group of 45 sick treated with pumpkin seed simultaneously with a small dose of atabrine, the tapeworm with scolex was expelled from 8 patients after one course of treatment (about 17·6 per cent). After two courses of treatment there were obtained positive results with 13 persons on the whole number of 22 sick (about 58·5 per cent).

" The above investigations show that after administering pumpkin seed twice at short intervals there were obtained results three times more successful than after one course of treatment. This seems to prove that pumpkin seed is more effective when longer operating. When applied together with atabrine the results, after one course of treatment, were but little better than that of pumpkin seed given alone. The results, however, after a second course of treatment proved to be much better.

" The obtained results seem to require a new, more exact technique of the pumpkin seed treatment, not so much by shock methods as by a long lasting administration of this remedy."

Pawlowski, Z. Wyniki leczenia *taeniarhynchosis* nasionami dyni (*Semina Cucurbitae*). [**Results of Treatment of Taeniasis with Pumpkin Seed** (*Semina Cucurbitae*). *Wiadomości Parazytologiczne*. Warsaw. 1956, v. 2, No. 2, 93–6. [15 refs.]

The English summary appended to the paper is as follows:—

" In 91 cases of taeniarhynchosis there was applied treatment by means of pumpkin seed (*Semina Cucurbitae*). According to the patients' age, 70–400 g seed and luminal (twice, in a dosage to 0·015 g) were given. As in most cases castor oil did not cause purgation within 4 hours there was additionally administered Carlsbad salt. The sick were controlled beginning from the fifth month after treatment. On 60 controlled persons 39 recovered, i.e. 65 per cent. Secondary symptoms were not observed. With regard to this remedy not being toxic there is, in cases of taeniarhynchosis, to be recommended the application of a pumpkin seed treatment, especially in conditions when the patient is not clinically attended to.

" As results from investigations hitherto carried out but not yet finished effective drugs against tapeworms seem to be tin preparations (24 sick on 26 proved to recover, i.e. 92·3%)."

Scotti, G. Cenni storici sulla imenolepiasi. [**Historic Data on** *Hymenolepis* **Infection**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1956, Mar., v. 37, No. 3, 127–31.

Zelman, S. *Echinococcus* **Disease in an American Veteran.** *U.S. Armed Forces Med. J.* 1955, Dec., v. 6, No. 12, 1800–806, 3 figs.

"An American veteran of World War II, presumably exposed to Echinococcus infection in North Africa in 1943 when he spent 2 months housed in a sheep barn, was found in 1955 to have a large hydatid cyst of the left lobe of the liver. Needle aspiration of the cyst, which is not advised, resulted in probable peritoneal soiling and the patient had an anaphylactic reaction. He was protected against what might otherwise have been a similar but more severe reaction by administration of adrenocortical steroids during and after operation."

Chakravarti, S. N. & Rastogi, A. K. **Subdiaphragmatic Abscess Secondary to Hydatid Cyst of the Liver.** *J. Indian Med. Ass.* 1956, Feb. 16, v. 26, No. 4, 142–3.

Picaro, A. Due casi di cisti da echinococco retroperitoneale. [**Two Cases of Retroperitoneal Echinococcal Cysts**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1956, Feb., v. 37, No. 2, 86–9.

Yamaguchi, T., Toyoda, H. & Murakami, K. [**On the Geographical Distribution of Hookworm in Shikoku Island. Part 1. Survey of Hookworm in Tokushima Prefecture**] *Shikoku Acta Med.* 1956, Jan., v. 8, No. 1, 7–11, 1 fig. [In Japanese.]

The English summary appended to the paper is as follows:—

"From Feb. 1953 to Apr. '55, the distribution of hookworm in Tokushima Prefecture was studied and as following results were obtained.

"1) By the treatment with tetrachloroethylene of about 350 infected persons, 293 were discharged hookworm and 262 or 89·4% were infected with *Ancylostoma duodenale*, 10 or 3·4% were with *Necator americanus* and 21 or 7·2% were with both species.

"2) A total of 4,120 specimens of hookworm were studied and 3,767 or 91·4% were *A. duodenale* and 353 or 8·6% were *N. americanus*.

"3) The 344 worms of *A. duodenale* demonstrated in one case, the most numerous infection."

Nunziante Cesàro, A., Granata, A. & Saitta, G. Analyse cytochimique du sang périphérique dans l'ankylostomiase. Observations sur le comportement cytochimique des granulocytes éosinophiles. [**Cytochemical Study of the Blood in Ankylostomiasis. Cytochemical State of Eosinophil Cells**] *Arch. Malad. Professionnelles.* Paris. 1956, Jan.–Feb., v. 17, No. 1, 19–24.

The authors have stained the formed components of the blood of 12 people suffering from ankylostomiasis. In addition to the usual polychromatic staining they stained for lipids, polysaccharides, ribonucleotides,

deoxyribonucleotides, peroxidase, oxidase and acid and alkaline phosphateses. No abnormalities were discovered. An interesting observation was that the alkaline phosphatase seemed to be largely in the cytoplasm whereas the acid phosphatase was more concentrated in the nuclei. The granules of eosinophil cells contained more phosphatase than other blood cells. They were not stained by any histochemical methods except by those which demonstrated both the phosphatases, and they were slightly positive when stained for peroxidases. *H. Lehmann*

Leslie, H. & Tovey, F. I. **Relation of Hookworm Infestation with Duodenal Ulcer.** *J. Indian Med. Ass.* 1955, Dec. 16, v. 25, No. 14, 548–51.

This study originated in the authors' interest in the association of ankylostomiasis with symptoms of duodenal ulceration. The differentiation of pure hookworm duodenitis from straightforward duodenal ulceration depends, it is stated, on examination of the stools for ova.

For the purpose of the study all male patients admitted to a hospital in Mysore, India, during a given period were considered. The incidence of hookworm infection in the whole series was the same as its incidence in patients proved to have duodenal ulceration, and the incidence of duodenal ulceration in the whole series was the same as its incidence in patients with hookworm infection. Duodenal ulceration was no more frequent in patients with ankylostomiasis than in controls and ankylostomiasis was no more frequent in patients with duodenal ulceration than in others. Compared with other areas no greater incidence of duodenal ulceration was found in those in which ankylostomiasis was especially prevalent—points which indicate that duodenal ulceration is not commonly caused by ankylostome infections.

The majority of patients with ankylostomiasis were symptomless, approximately 20 per cent. had symptoms of duodenitis and between 13 and 17 per cent. had less than 60 per cent. haemoglobin. Pain associated with duodenitis attributed to ankylostomiasis was usually less periodic and of shorter duration than in uncomplicated duodenal ulceration—3–12 months, compared with 1–10 years. Tenderness was more diffuse and anthelmintic treatment gave dramatic relief from pain.

It is suggested that genuine duodenal ulceration may be recognized in patients suffering from ankylostomiasis by this greater duration of symptoms, the response to anthelmintic treatment, the tendency to periodicity, a high gastric acidity, localization of tenderness and persistent instead of fleeting deformity of the duodenal cap as visualized during barium meal examination. *A. W. Woodruff*

Lippi, M. Ulteriore contributo della terapia dell'anchilostomiasi con associazione di exilresorcinolo e tetracloroetilene per instillazione

duodenale. [**Further Observations on the Treatment of Ankylostomiasis with a Combination of Hexylresorcinol and Tetrachlorethylene given through a Duodenal Tube**] *Arch. Ital. Sci. Med. Trop. e Parassit.* 1956, Feb., v. 37, No. 2, 57–9. [10 refs.]

[See this *Bulletin*, 1955, v. 52, 915.]

Gillet, J., de Smet, R. M. & Nannan, P. L'action thérapeutique favorable d'un dérivé du thioxanthone (Nilodin) dans la strongyloïdose. [**The Favourable Therapeutic Action of a Derivative of Thioxanthone (Nilodin) on Strongyloidiasis**] *Ann. Soc. Belge de Méd. Trop.* 1955, Oct. 31, v. 35, No. 5, 499–503. [14 refs.]

The authors treated 242 adult African patients infected with *Strongyloides stercoralis* with a derivative of thioxanthone sold under the name Nilodin. Patients were examined during treatment and for 14 days after this ended, this period being chosen because the incubation period of infection with *S. stercoralis* is 15 days. Each examination included 3 direct smears from the faeces and, if these were negative, concentration methods were used. The Telemann method was soon given up, because the authors could not tell whether the larvae had been killed by the acid and ether or by the Nilodin. For reasons of convenience they abandoned Faust's zinc sulphate method in favour of simple successive centrifugations and examination of the final deposit. Results were classified as (a) living rhabditoid larvae found; (b) rigid, straight and inert rhabditoid larvae found; (c) no larvae found. Patients were considered cured when no living or immobile larvae were found during 14 days after treatment.

The first series of 68 patients were given doses varying from 5 to 20 mgm./kgm. daily in divided doses for 6 days by the mouth. A table shows that daily doses of 15 to 20 mgm./kgm. gave 93·7 or 100 per cent. of cures.

A second series of 174 patients each received by the mouth daily doses of 12 to 20 mgm./kgm. for 2 days only. A table shows that 16 mgm./kgm. given to 60 patients gave 95 per cent. of cures, while 18 mgm./kgm. given to 42 patients gave 92·8 per cent. of cures and 20 mgm./kgm. given to 50 patients gave 98 per cent. of cures.

Both the 2-day and 6-day courses were well tolerated and both seemed to produce their results after 2 days. Nilodin had no effect in *Taenia*, *Ascaris*, *Trichuris* or ankylostomes. The authors conclude that the derivatives of thioxanthone sold under various proprietary names seem to have a distinct action on *Strongyloides stercoralis*. *G. Lapage*

Alwa, R. V. K. **Acute Gangrenous Appendicitis caused by Roundworms.** *J. Indian Med. Ass.* 1956, Mar. 16, v. 26, No. 6, 235.

Basnuevo, J. G., Blanco Rabassa, E., Mañas, A. & Casanova, R. Cuarenta casos de Ascariasis tratados con Adipato de piperacina. [**Forty Cases of Ascariasis treated with Piperazine Adipate**] *Rev. Kuba Med. Trop. y Parasit.* 1955, Jan.–June, v. 11, Nos. 1/6, 3–5.

The dose was 50 mgm./lb. daily for 7 days, with a maximum daily dose of 4 gm.; 33 of 40 patients were cured.

Basnuevo, J. G., Mañas Cao, A. & Casanova, R. Un nuevo tratamiento de la Ascariasis. [**A New Treatment of Ascariasis**] *Rev. Kuba Med. Trop. y Parasit.* 1955, Jan.–June, v. 11, Nos. 1/6, 14–16, 4 figs.

The authors describe and illustrate the successful use of piperazine hexahydrate or adipate in the treatment of ascariasis.

Bhaskaran, T. R., Sampathkumaran, M. A., Sur, T. C. & Radhakrishnan, I. **Studies on the Effect of Sewage Treatment Processes on the Survival of Intestinal Parasites.** *Indian J. Med. Res.* 1956, Jan., v. 44, No. 1, 163–80, 7 figs. [11 refs.]

To the pathogenic organisms of sewage in the temperate zones, the tropics and sub-tropics add the hazard of intestinal parasites. This paper describes investigations of the effectiveness of 5 methods of treating sewage in removing intestinal parasites. The index organisms used were ova of *Ascaris*, hookworm and *Trichuris*. The treatment methods tested were activated sludge in a municipality near Calcutta (not very well operated), activated sludge in a small industrial community, septic tank followed by a contact bed, an experimental trickling filter and an experimental septic tank.

Samples of sewage from Calcutta city and from the 3 communities under investigation showed heavy infection with intestinal parasites, ranging from over 22,000 per person per day to nearly 220,000, mainly *Ascaris*. In the standardized laboratory technique finally adopted for recovering and counting the parasitic ova a 600-cc. (or larger) sample of sewage was taken and allowed to settle overnight at below 4°C. The supernatant was decanted and 100 cc. of sediment taken up in saturated salt solution. At the end of an hour in a narrow cylinder the helminth ova had floated to the surface; 10 cc. of the top layer were carefully removed by pipette and the eggs were counted in a Whipple cell. Sludge under investigation was suspended in water and the same procedure adopted. The viability of ova in sludge was determined by culturing (at room temperature) the samples in normal saline containing 5 per cent. formalin. Samples were taken from this culture medium at various time intervals and examined for the presence of embryos in the eggs.

The efficiency of removal of the treatment processes investigated varied quite widely. Plain settling for about 2 hours removed 50–70 per cent. of the ova. A well-operated septic tank, with 3 days' retention, was more effective, giving an effluent with less than 2 eggs per gallon. The authors, however, consider that more data are necessary on the septic tank. The septic tank followed by contact bed removed 70–80 per cent. of the ova; final chlorination removed about 98 per cent. Both trickling filters and activated sludge, when properly operated and maintained, are about equally efficient, showing almost complete removal of parasite ova.

The data presented in the paper emphasize the importance of good maintenance and operation of sewage-treatment plant. None of the sewage-treatment processes ordinarily used (*i.e.* without terminal chlorination) remove helminth ova completely. The authors point out that, in the absence of data on the minimum insult necessary to produce infection, it is not possible to be sure that this treatment is adequate. They believe, however, that no great hazard will be caused by using these treated effluents for irrigation of suitable crops. *Peter C. G. Isaac*

Briceño Rossi, A. L. El problema de la Wuchereriasis bancrofti en Venezuela. Introduccion—historia—geografia—parasitologia—epidemiologia—patologia—intra-dermo reaccion—tratamiento y pautas de erradicacion. [**The Problem of** *Wuchereria bancrofti* **Infection in Venezuela**] *Rev. Sanidad y Asistencia Social.* Caracas. 1952, Jan.–Apr., v. 17, Nos. 1/2, 1–120, numerous pls. [Numerous refs.]

Ferreira, M. O., Rachou, R. G., Martins, C. M. & Ferreira Netto, J. A. Novo foco de filariose bancroftiana no sul do Brasil; Barra, Município de Laguna, Estado de Santa Catarina. [**New Focus of** *Wuchereria bancrofti* **Infection in South Brazil (Barra, Santa Catarina)**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, July, v. 7, No. 3, 325–8. English summary (5 lines).

Rachou, R. G. Variação da microfilaremia de *Wuchereria bancrofti* em 25 portadores em Santa Catarina examinados durante 52 semanas seguidas. [**Variation of Microfilaraemia in** *W. bancrofti* **in 25 Carriers in Santa Catarina, Brazil, examined for 52 Consecutive Weeks**] *Rev. Brasileira Malariologia.* Rio de Janeiro. 1955, Apr., v. 7, No. 2, 209–13.

The English summary appended to the paper is as follows:—

"The author examined, once a week, during 52 weeks, the blood (20 c.mm., collected from 8 p.m. to 11 p.m.) of 25 carriers of microfilariae of *W. bancrofti*, residents in the State of Santa Catarina, Brazil, where the seasons of the year are well defined. He found a great weekly

variation of the microfilariae density. Among 1,297 blood samples, 21·2% were negative for microfilariae, although, theoretically, 100% ought to be positive. In autumn-winter microfilariae density was higher than in summer-spring. To the months of higher microfilariae density corresponded the months of lower density of the vector (*C. p. fatigans*), of lower temperature and of earlier sunset. The author thinks that the observed higher density of microfilariae should be related to the last factor, the earlier sunset determining an earlier hour to go to bed. In the interpretation of several bancroftiasis surveys carried out in the south of Brazil, the epidemiologist has to consider this seasonal variation to analyse microfilariae density as an epidemiological rate."

Leví-Castillo, R. Estudios sobre *Culex pipiens quinquefasciatus* en la ciudad de Guayaquil—Morfología de los machos en razas resistentes y no resistentes, a los insecticidas clorados biometría y técnicas usadas. [**Studies on *Culex fatigans* in Guayaquil, Ecuador. Morphology of Males in Strains Resistant and Non-Resistant to Chlorinated Hydrocarbon Insecticides**] *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1954, Jan.–Apr., v. 2, Nos. 1/2, 7–13, 10 figs.

The English summary appended to the paper is as follows:—

" Biometrical measures are made on male specimens of Culex pipiens quinquefasciatus that had been previously artificially made resistant to DDT, Gammexane and Chlordane and observations effected gave as a result a shrinkage in measures as the generations became more and more resistant by successive treatments of insecticides."

See also p. 936, Blazquez & Maier, Ginandromorfismo en *Culex fatigans* sometidos por generaciones sucesivas a exposiciones de DDT. [**Gynandromorphism in *Culex fatigans* exposed to DDT for Successive Generations**]

Mirsa, A., Mirsa, Marie & Ortiz, I. Primer hallazgo de formas evolutivas de microfilarias en el tórax de *Culicoides* (*C. pifanoi* Ortiz, 1951) en Venezuela. [**First Record of Developing Forms of Microfilariae in the Thorax of a *Culicoides* (*C. pifanoi*) in Venezuela**] *Rev. Sanidad y Asistencia Social.* Caracas. 1952, Jan.–Apr., v. 17, Nos. 1/2, 159–62. [15 refs.]

The following is a translation of the authors' summary:—

The authors record the finding of developing forms of microfilariae in the thoracic muscles of a female specimen of *Culicoides pifanoi*, coming from the environs of San Felipe in the State of Yaracuy.

H. J. O'D. Burke-Gaffney

García-Solórza, E. & Leví-Castillo, R. Filariasis en el mono *Cebus albifrons aequatorialis* de la Región Litoral del Ecuador (Nota Previa). [**Filariasis in the Monkey** *Cebus albifrons aequatorialis* **in the Coastal Region of Ecuador**] *Rev. Ecuatoriana de Entom. y Parasit.* 1954, Jan.–Apr., v. 2, Nos. 1/2, 101–4, 5 figs. on 2 pls.

The English summary appended to the paper is as follows:—

"The authors describe for the first time the presence of microfilariae in the liver tissue of the monkey *Cebus albifrons aequatorialis*, that is a very common species of primate in the virgin jungles of the coastal plain of Ecuador. The presence of microfilaria is well illustrated with photographs of the liver tissue with the parasites, the species of which is not yet determined, being thus a necessity to study more material and of preparing cultures of the parasite in order to be able to determine to which species does it belong. Presence of a patient with typical symptoms of the disease gives importance to the fact that it may be extended, yet unnoticed in the coastal plain in Ecuador."

Briceño Rossi, A. L. Primeros casos de filariasis a Manzonella ozzardi constatados en Venezuela. [**First Cases of** *Mansonella ozzardi* **Infection Recorded in Venezuela**] *Rev. Sanidad y Asistencia Social.* Caracas. 1949, Sept.–Dec., v. 14, Nos. 5/6, 671–4.

Duke, B. O. L. **Studies on the Biting Habits of** *Chrysops*. **III.—The Effect of Groups of Persons, Stationary and Moving, on the Biting Density of** *Chrysops silacea* **at Ground Level in the Rain-Forest at Kumba, British Cameroons.** *Ann. Trop. Med. & Parasit.* 1955, Dec., v. 49, No. 4, 362–7, 1 fig. **IV.—The Dispersal of** *Chrysops silacea* **over Cleared Areas from the Rain-Forest at Kumba, British Cameroons.** *Ibid.*, 368–75, 1 map & 2 figs.

III. In the first paper the number of *C. silacea* caught by stationary groups of 8 and 16 fly-boys was compared with the number caught by single stationary fly-boys [this *Bulletin*, 1955, v. 52, 1124; 1956, v. 53, 352]. More flies were attracted by groups of boys. The daytime biting curve recorded by groups of fly-boys resembled more closely the biphasic curves recorded by single fly-boys at ground level with a fire, or at canopy level without a fire, and did not show the very low morning levels followed by a rise in the mid-afternoon recorded by single fly-boys at ground level without a fire. It is suggested that the group attracts flies down from the forest canopy. Comparison of flies caught by stationary and moving groups of fly-boys showed that while a group is moving it is subject to a slightly lower biting density, but once it has halted it is subject to a slightly higher biting density. It is suggested that flies follow a group that is moving and bite mainly when it is stationary. Troops of drills [*Mandrillus*], which are potential reservoirs

of *Loa loa*, move about the forest, but captive animals have been observed to catch and eat all visiting *C. silacea*.

IV. The second paper shows that the biting density of *C. silacea* visiting single fly-boys with a wood fire in clearings decreased logarithmically with increasing distance from the edge of the rain forest. Biting density was measured in two areas, one of which was a cleared area planted with rubber 1½–2 feet high, and the other a cleared area planted with rubber 10–12 feet high. In each area a forest station and, in the clearings, stations at known distances (up to 400 yards) from the forest edge were set up, all the stations lying along a straight line bisecting a corner of each clearing. The daily catch at each station in each clearing was expressed as a proportion of the catch on the same day in the corresponding forest station. The mean proportional catch at each station with the calculated 95 per cent. confidence limits were then recorded. By plotting the logarithms of these against distance from the forest edge 3 straight lines are produced, the upper and lower of which represent the upper and lower confidence limits. These lines (represented by $-\log y = kx$, where y is the mean proportional catch and x distance from forest edge) were used to discover the distance, with confidence limits, at which the biting density (represented by mean proportional catch) fell to one-tenth of the forest-station value. In the area of low vegetation the distance at which the biting density was one-tenth of the forest station was 100 yards (with confidence limits of 36–171 yards), whereas in the area with tall rubber trees the corresponding figure (by extrapolation) was 530 yards (222–1,326 yards). It is suggested that the taller trees provided sufficient shade and resting places, enabling the flies to penetrate further from the forest. Relatively narrow ruthless barrier clearings, 100–200 yards wide, may be sufficient to prevent *C. silacea* penetrating from its breeding areas into areas where the flies can feed readily on man. *B. R. Laurence*

Nicholas, W. L., Kershaw, W. E. & Duke, B. O. L. **Studies on the Epidemiology of Filariasis in West Africa, with special reference to the British Cameroons and the Niger Delta. VII.—Further Records of the Distribution of *Culicoides* spp., with a Note on the Taxonomic Status of *C. austeni*.** *Ann. Trop. Med. & Parasit.* 1955, Dec., v. 49, No. 4, 455–60, 1 map. [16 refs.]

Culicoides austeni was originally differentiated from *C. milnei* by possessing contiguous eyes, the two distal costal pale spots being closer together, the second radial cell narrower, and the macrotrichia extending nearer to the base of the wing [this *Bulletin*, 1921, v. 18, 199]. Examination of specimens of both species, including the type series, shows that the two species cannot be separated on these characters and that *C. austeni* is a synonym of *C. milnei*.

The present records confirm the belief that *C. milnei* and *C. grahami* are common throughout rain forest in the British Cameroons and S. Nigeria. *C. milnei* is also recorded from savannah in N. Nigeria, including the Bauchi plateau area, where infection with *Dipetalonema perstans* is common locally. *C. inornatipennis* appears to be confined to rain forest whereas *C. nigeriae*, which is very similar, is confined to drier grasslands. Previous records of *C. inornatipennis* from Ndop, British Cameroons [this *Bulletin*, 1953, v. 50, 748] refer to *C. nigeriae*. *C. inornatipennis*, *C. nigeriae* and *C. grahami* generally bite shortly before dusk and after sunrise, occasionally biting throughout the day. *C. milnei* in N. Nigeria shows the same biting behaviour as elsewhere.

C. milnei, *C. inornatipennis*, *C. grahami*, *C. fulvithorax* and *C. bwambanus* are recorded as breeding in rotting banana and plantain material, *C. quinquelineatus* in rotting vegetable refuse and rotting plantain stems, *C. neavei* in soil at the base of a forest tree, *C. bwambanus* in rot-hole material, and *C. grahami*, *C. fulvithorax* and *C. confusus* in wet mud at the base of elephant grass. No bananas or plantains were growing in the areas of N. Nigeria (Bukuru, Song) where *C. milnei* was collected. *B. R. Laurence*

Dalmat, **The Black Flies (Diptera, Simuliidae) of Guatemala and their Role as Vectors of Onchocerciasis.**

This book was reviewed on p. 518.

See also p. 932, Weyts, **Ocular Manifestations in Onchocerciasis.**

Pistoletti, G. Indagini sulla incidenza della ossiuriasi in provincia di Pisa e sulla possibilità di una bonifica di massa. [**Investigations on the Incidence of Enterobiasis in Pisa Province and on the Possibility of Mass Treatment**] *Ann. d. San. Pubblica.* Rome. 1955, Sept.–Oct., v. 16, No. 5, 1117–25, 1 folding fig. [19 refs.] English summary (7 lines).

In view of the very wide distribution of *Enterobius* infection reported by so many workers, the author decided to investigate the incidence in children 5–11 years of age in residential schools in Pisa province, using the " cellulose tape slide " (CTS method) of the Communicable Disease Center of Atlanta, U.S.A.

The following results were obtained:—

Sex	*Patients*	*Number positive*	*% positive*
F	606	253	41·7
M	717	325	45·3

He found, as other authors have done, that the percentage of subjects infected increased progressively with the age of the children.

He then decided to try the effect of treatment, using Egressin and piperazine. Egressin is isopropyl-m-cresyl-isoamylcarbamate, and the piperazine used was the hydrate. Two groups of children aged 5–8 years were chosen, and to one, 3 tablets of Egressin daily for two days were given, each tablet containing 0·9 gm. of the ester. The piperazine was given in a syrup, each cc. containing 0·85 gm. of the salt, with a dosage of 1 cc. per year of age 3 times daily, in two cycles of 7 gm. each with a week's interval between. In all, 39 children were treated with Egressin, and 22 with piperazine, and on follow-up 5, 15 and 30 days later by means of the CTS method, 66·6 per cent. of the former were cured, and 90·9 per cent. of the latter. No ill effects were found in the children treated with piperazine, but some of those treated with Egressin had either urticaria, or abdominal pain.

The treatment was given at home or in the residential school and appropriate instructions were given to the mothers or teachers on general hygienic measures designed to prevent reinfection.

The author considers that piperazine lends itself well to mass treatment if combined with adequate propaganda and measures of general hygiene. *W. K. Dunscombe*

Themann, H. Die experimentelle Rattentrichinose unter dem Einfluss von Calciumbehandlung. [**Experimental Trichinosis of the Rat in Relation to Treatment with Calcium**] *Ztschr. f. Parasitenk.* 1956, v. 17, No. 4, 300–329, 10 figs. [Numerous refs.]

DEFICIENCY DISEASES

Food and Agriculture Organization of the United Nations. **FAO Nutritional Studies No. 1. Rice and Rice Diets. A Survey prepared by the Nutrition Division.** pp. v + 78. [100 refs.] Rome: 1954, Sept. (Revised Edition). [Sales Agent for U.K., H.M. Stationery Office.] [$0.75; 3s. 9d.]

Food and Agriculture Organization of the United Nations. **FAO Nutritional Studies No. 9. Maize and Maize Diets. A Nutritional Survey.** pp. iii + 94, 3 figs. [173 refs.] Rome: 1954, Feb. (2nd printing). [Sales Agent for U.K., H.M. Stationery Office.] [$1.00; 5s.]

The FAO Nutritional Studies form an excellent series of monographs providing valuable information for nutrition workers. The fact that a

revised edition of No. 1 and a second printing of No. 9 have been necessary is satisfactory evidence that they are being used and appreciated. The two monographs give detailed information of the chemical and biological properties of rice and maize, of the differences in the botanical variations of each cereal and of the effects of the various preparations made from them for human consumption. The properties of the 2 cereals are fully discussed in relation to the other foods usually found in the diets of rice and maize eaters. The deficiencies in essential nutrients which are liable to arise in such diets are fully set out, the possible effects on health are discussed and practical ways and means for improving the diets are suggested.

Both monographs are written in clear and simple language, and are essentially practical handbooks. However, each contains full references to the literature and a discussion of the complicated biochemical problems associated with the relative deficiencies of specific nutrients in each cereal. Thus they can be recommended both to experienced research workers and to field workers engaged in attempts to improve the health of the large rural populations who subsist essentially on these 2 cereals. Indeed no one who is actively concerned in the welfare of the people in countries where either of these two cereals are the staple food can afford to be without one or other of these admirable scientific guides to their practical problems. *R. Passmore*

Gounelle, H. Déficits nutritionnels en Moyen-Orient. [**Nutritional Deficiencies in the Middle East**] *Bull. Acad. Nat. Méd.* 1956, v. 140, Nos. 5/6, 79–82, 1 chart.

This paper gives a very brief account of the nutritional state of the people of Iraq, emphasizing the impaired growth rates of young children especially in the second year of life, a general insufficiency of food among the adult population for sustained physical effort, and widespread anaemia due to iron deficiency and aggravated by ankylostomiasis and schistosomiasis. Aided by FAO a National Nutrition Committee has been set up with representatives of Public Health, Agriculture, Education, Social Affairs and Defence Services: this committee will, it is hoped, play a notable part in educating the people through the press, the radio and the schools. A National Nutrition Institute is being set up under a Medical Director. A clinical section will have 24 beds. There will also be a section for field investigations and 2 laboratory sections, one for food analyses and the other for biochemical determination in man. The United Nations is aiding in the training of the staff of the Institute. Four doctors and 3 biochemists have been allotted fellowships for study in France. *R. Passmore*

See also p. 946, VAN DER HOEVEN, J. A., Resultaten van een onderzoek naar voeding en deficientie-verschijnselen bij autochthone zuigelingen in Nederlands Nieuw-Guinea. [**Results of a Nutritional and Medical Survey of Autochthonous Infants in Dutch New Guinea**]

HUANG, Po-chao & TUNG, Ta-cheng. **Nutritional Status of the Normal Schools Students.** *J. Formosan Med. Ass.* 1955, Oct., v. 54, No. 10, 329–36.

A rice enrichment project has been carried out in 3 normal schools in Formosa and the effects examined on 2,255 students aged 15–21 years for 3 months. During the period the incidence of angular stomatitis fell in 3 schools from 57 to 34 per cent., from 27 to 8 per cent. and from 45 to 17 per cent.; in a school not receiving enriched rice the incidence of angular stomatitis was 52 per cent. at the beginning and 45 per cent. at the end of the experimental period. There was a marked increase in urinary excretion of thiamine and riboflavine by those on the enriched rice. [Unfortunately the table giving the basic diets of the schools, which is referred to in the text, has not been included in the paper. Without these details of the students' diet, it is difficult to judge the significance of the results.] *R. Passmore*

PELLETT, P. L. & PLATT, B. S. **A Dietary Defect in Maize developed during Treatment with Lime.** *Nature.* 1956, Mar. 3, v. 177, 422–4. [14 refs.]

The rate of growth of rats fed on lime-treated maize was significantly lower than that of rats fed on untreated maize. The addition of either nicotinic acid or tryptophan had no effect on this depressed growth rate. With the addition of either aureomycin or a mixture of B vitamins, the growth of the rats was the same on treated and untreated maize. These results are discussed in relation to the epidemiology of pellagra. Pellagra is not common in some parts of Mexico, where the maize is treated with lime in the making of tortillas. There have been conflicting reports of the effect of lime treatment on the nutritive value of maize for rats. BRAUDE *et al.* [this *Bulletin*, 1955, v. 52, 814] found that maize after partial hydrolysis with sodium hydroxide had a curative effect on pellagra in pigs, which they attributed to liberation of bound nicotinic acid. Clearly there are still unsolved problems in the relationship between maize and pellagra. These are discussed more fully in this paper.

R. Passmore

Ferro-Luzzi, G. Il problema dell'adeguamento proteico della dieta nelle zone economicamente depresse. [**The Problem of a Protein Sufficiency of the Diet in Economically Depressed Areas**] Reprinted from "Atti" del: 2°Symposium sulla fisiopatologia dell'alimentazione, Roma, 27–29 gennaio 1955. *Ricerca Scientifica.* 1955, v. 25, Suppl., 28 pp. English summary.

It has been assumed that for the well-being and good health of the human race the individual daily diet should include the "standard" equivalent of 70 gm. of protein per male adult, and that a sufficiency of this protein should be of animal origin. But more than half the world population is consuming the equivalent of only 50 gm., and little of this protein is of animal origin. Much of the illness and of the inferior health which is prevalent among the people of underdeveloped or economically depressed countries has been widely attributed to protein deficiency in their diet, but the author is not satisfied that a causative relationship has yet been demonstrated scientifically and beyond doubt, and it would be premature to embark on such a major and costly undertaking as that of providing all people with a diet which includes the equivalent of 70 gm. of the appropriate quality protein per male adult per day. This figure of 70 gm. has been arrived at by adding a presumptive safety margin to what is considered to be the minimum.

Can we rely on the diagnostic means (clinical, laboratory and statistical), which we can dispose of at present, to demonstrate individual cases of protein deficiency other than those of infant or otherwise severe type? Though a lower intake of protein, and more particularly of animal protein, is certainly an index of mass poverty in many underdeveloped areas, it is far from easy to verify that a community is suffering from mass deficiency of protein, quantitative and qualitative, in their diet. It is even more difficult to prove that mass ill-health and low productivity are due to lack of an appropriate protein diet.

The author refers to his experience in East Africa and compares the superior stature (average adult height of 165 cm.) of Eritreans, whose average daily intake of protein is equivalent to 50·5 gm., with the physical development of Eskimos, whose diet is one of the richest in protein, and with the Chinese, whose daily intake is equivalent to 65·7 gm. of protein (1947–48 survey of 22 provinces by FAO).

J. Cauchi

McCarthy, D. D. **Liver Enlargement and Protein Deficiency States in Polynesians in Western Samoa, Niue, and New Zealand.** *New Zealand Med. J.* 1955, Dec., v. 54, No. 304, 651–7, 1 fig. & 3 graphs. [22 refs.]

Symptomless enlargement of the liver was found in 7 per cent. of children examined in Niue, and in 8 to 15 per cent. in different groups of children in Western Samoa. The incidence was higher in boys than in

girls and greatest between the age of 3 and 4. These findings confirm dietary evidence that throughout Samoa and Niue there is a widespread deficiency of protein in the diet of the children.

Enlargement of the liver was also found in up to 7 per cent. of the Maori children below the age of 4 years in New Zealand. Faulty habits during the weaning period and the possible presence of protein malnutrition in some Maori mothers during the later months of pregnancy may be responsible. *R. Passmore*

HAEMATOLOGY

Devignat, R. & Dresse, A. Petites facilités techniques en hématologie. [**Some Simplified Haematological Techniques**] *Ann. Soc. Belge de Méd. Trop.* 1955, Oct. 31, v. 35, No. 5, 491–5.

Working on rats, the authors have developed some techniques which they publish for the benefit of other workers. The first two are concerned with the measurement of blood and bone-marrow components on a microscale. The principle is that on addition of anti-coagulant, blood as well as marrow alters its viscosity and can be more easily taken up into small glass capillaries, or will more rapidly centrifuge in small appliances. The third modification concerns the staining of blood cells. The "panoptical" staining of these cells is based on their content of an eosin-methylene blue mixture. The authors suggest that the 3 constituents of this stain should be prepared separately, and that they can then be mixed according to requirement. The following mixture is, for instance, much less rich in methylene blue and eosin than the commercial Giemsa stain:

Distilled water buffered at *p*H 6·8	10 ml.
Azur eosinate I	40 minims [*gouttes*]
Methylene blue solution	3 minims
Eosin solution	1 minim

H. Lehmann

Girdwood, R. H. **The Megaloblastic Anaemias. Their Investigation and Classification.** *Quart. J. Med.* (n.s.). 1956, Jan., v. 25, No. 97, 87–119, 3 figs. [47 refs.]

Thomas, E. D. **The Treatment of Refractory Anemia with Cobalt.** *Ann. Intern. Med.* 1956, Feb., v. 44, No. 2, 412–19, 2 figs. [13 refs.]

"A case is reported of macrocytic refractory anemia with cellular bone marrow that responded to cobaltous chloride therapy. The value of cobaltous chloride in refractory anemia is discussed."

Ortiz Rivas, E. & Vegas, F. Estudio sobre las hemoglobinas. 1. La electroforesis en papel en las hemoglobinopatías hereditarias. [**Study of Haemoglobins, I: Electrophoresis on Paper in Hereditary Haemoglobin Diseases**] *Rev. Cubana Lab. Clin.* 1956, Jan.–Feb.–Mar., v. 10. No. 1, 36–52, 6 figs. [53 refs.]

Siddoo, J. K., Siddoo, S. K., Chase, W. H., Morgan-Dean, L. & Perry, W. H. **Thalassemia in Sikhs.** *Blood.* 1956, Mar., v. 11, No. 3, 197–210, 10 figs. [32 refs.]

"1. The incidence of Thalassemia minor in the Sikh community of Vancouver, Canada, was computed to be six per cent from a study of 80 individuals, of whom five showed this condition.

"2. To determine the incidence in blood relatives, the families of the above five propositi were then studied in detail. In addition, a sixth family, that of the original propositus was included. This made a total of 79 individuals, of whom 38 had Thalassemia minor and none had Thalassemia major.

"3. It is suggested that a large pool of the Thalassemia gene existed in the Mediterranean basin and perhaps spread to Italy, Greece, Syria, Kurdistan, India, Thailand and China, countries which lie along the routes of early migration of races."

Derrien, Y. & Reynaud, J. Etude comparée des hémoglobines humaines normales et pathologiques par électrophorèse en veine liquide en tampon cacodylique dilué. Dictinction des hémoglobines d'anémiques de Cooley et de nouveau-nés. [**Comparative Study of Normal and Pathological Human Haemoglobins by Electrophoresis in Diluted Cacodylate Buffer; Differentiation between Haemoglobins in Thalassaemia and in New-Born Infants**] *C.R. Soc. Biol.* 1955, Aug.–Sept., v. 149, Nos. 15/16 & 17/18, 1595–1602, 6 figs.

Pauling *et al.* showed in their classical experiment [*Science*, 1949, v. 110, 543; this *Bulletin*, 1950, v. 47, (267)] that adult haemoglobin moved as a single component in open boundary electrophoresis, but that sickle-cell-trait carriers had a haemoglobin which could be resolved into two components: normal adult haemoglobin, and sickle-cell haemoglobin. By altering the concentration of the buffer from ionic strength 0·1 to 0·019 the authors have obtained different results. Adult haemoglobin was resolved into at least 3 different components, and sickle-cell haemoglobin and haemoglobin C into two components each. They also obtained different mobilities with alkali-resistant haemoglobin from new-born infants and from thalassaemia patients. The following table summarizes their results.

Constituents	Source	Mobility at 2°C. 10^{-5}cm.^{2}; volt^{-1}; sec.$^{-1}$.
1	Accompanying protein (?)	+ 1·7
2	Accompanying protein (?)	+ 4·4
2′	Alkali res. Hb. thalassaemia	–
3	Alkali res. Hb. thalassaemia and adult Hb.	+ 5·0
4	Adult Hb.	+ 5·1
4′	Adult Hb.	–
5, 5′	Alkali res. Hb. infants and sickle-cell Hb.	+ 5·2
6	Sickle-cell Hb.	+ 5·8
7	Haemoglobin C	–
8	Haemoglobin C	+ 7·5

[These results, which incidentally do not invalidate any genetical conceptions as regards the inheritance etc. of these haemoglobins, are of interest, particularly in view of the finding of a haemoglobin-E-like component in normal adults and in increased amounts in thalassaemia minor which has been reported by Kunkel and Wallenius (*Science*, 1955, v. 122, 288).] *H. Lehmann*

Didier, R. & Diacono, G. Enquête sur la sicklémie en Tunisie. [**Survey of Sicklaemia in Tunisia**] *Arch. Inst. Pasteur de Tunis.* 1956, Mar., v. 33, No. 1, 61–4.

The authors examined 820 children, representative of the Tunisian population, for evidence of sickling. They found 16 (2 per cent.) positive. This is claimed to be the first such record in Tunisia. No cases of sickle-cell anaemia were found, but the authors point to the need for more extensive studies in this direction, both from the pathological and anthropological aspects. *H. J. O'D. Burke-Gaffney*

Griggs, R. C. & Harris, J. W. **The Biophysics of the Variants of Sickle-Cell Disease.** *Arch. Intern. Med.* 1956, Mar., v. 97, No. 3, 315–26, 7 figs. [29 refs.]

"The data presented here support the theory that (1) the sickling phenomenon plays a critical role in the pathogenesis of many of the symptoms seen in sickle-cell disease and in the shortened life span of sickle cells; (2) the severity of both the circulatory alterations and anemia is related to the response of the sickle cell to changes in oxygen tension; (3) this response is mainly dependent upon the intracellular concentration of sickle hemoglobin."

Harris, J. W., Brewster, H. H., Ham, T. H. & Castle, W. B. **Studies on the Destruction of Red Blood Cells. X. The Biophysics and Biology of Sickle-Cell Disease.** *Arch. Intern. Med.* 1956. Feb., v. 97, No. 2, 145–68, 9 figs. [60 refs.]

This article deals with the physical phenomena of sickling and demonstrates that our present knowledge suffices to understand the development of sickle-cell crises. It is known that sickling is caused by the low solubility of reduced sickle-cell haemoglobin, thus the cells from patients with sickle-cell anaemia which contain largely sickle-cell haemoglobin begin to show sickling shape when the oxygen saturation of the haemoglobin is within the range of 60–90 per cent.; at 40 per cent. saturation 75 per cent. or more of the cells are in sickle form. In contrast to this, cells from sickle-cell trait begin to sickle only at 30–50 per cent. oxygen saturation. Not until 20 per cent. oxygen saturation has taken place are 75 per cent. of the cells sickled. Another effect of deoxygenation on sickle-cell blood is an increase in viscosity. At 40 per cent. saturation all anaemia samples investigated show 85 per cent. or more of their maximal increase in viscosity. The increase in 4 out of 5 trait samples is less than 10 per cent. at this oxygen saturation.

The third difference between anaemia and trait is in osmotic and mechanical fragility; particularly after a 24-hour sterile incubation a great difference can be shown. The majority of sickle-cell anaemia cells show an increased resistance to osmotic lysis well outside the normal range. Cells from persons with the sickle-cell trait show only a slightly increased osmotic resistance. In addition to an increase of resistance shown by the majority of the anaemia cells a proportion show after incubation an abnormally decreased resistance, whereas the sickle-cell trait cells do not show this phenomenon. An increased osmotic resistance usually indicates that an erythrocyte is flat and poorly filled with haemoglobin, so that more water can enter the cell before lysis takes place at the critical spherical form. However, in sickle-cell anaemia the cells are not flat, nor are they poorly filled with haemoglobin and the authors suggest that the explanation is an alteration of the cell membrane permitting loss of osmotically active substances. Another explanation is put forward for the finding in the anaemia of a small number of cells with decreased resistance. Cells which show an increased fragility are assumed to be more nearly spherical than normal cells. Such an increase in spheroidicity of normal erythrocytes is produced *in vitro* by incubation procedures and the authors suggest that the sickle-cell anaemia cells which show this increased osmotic fragility are those which have been selectively sequestrated and in effect incubated *in vivo*. Such selective sequestration of anaemia erythrocytes has been demonstrated to occur in the spleen and it has been shown that after sequestration these cells remain irreversibly sickled. The mechanical fragility is much greater in sickled cells than in non-sickled cells. If the red cells are fully oxygenated no difference is seen, but with slight falls of oxygen tension

the different mechanical fragility parallels the difference in the degree of sickling.

Thus there are 3 main points one can make as regards sickling in sickle-cell anaemia and in related conditions:

1. *Sickling*: The alignment and parallel orientation of the abnormal haemoglobin molecule in its insoluble deoxygenated state results in the formation of tactoids. Because of this intracellular molecular orientation the cell assumes the sickled form. "The birefringent sickled erythrocyte is essentially a membrane-covered haemoglobin tactoid."

2. *Infarction*: Owing to the abnormal form of the erythrocytes the viscosity of the whole blood and the mechanical fragility of the erythrocytes are significantly increased at decreased oxygen tensions. The increase in viscosity initiates a cycle in which stasis, lowered *p*H and continued oxygen uptake by the tissues augment the number of sickle cells and prolong the stasis, hence infarction and venous thrombosis occur.

3. *Haemolytic anaemia*: When red cells after stasis are released from their incubation and return into free circulation a certain number have been fixed irreversibly in their sickled form and will thus show an increase in osmotic and mechanical fragility as a result of stasis. The operation of this cycle appears to explain in large part the clinical manifestations of sickle-cell disease, thus the abnormalities of the erythrocytes are responsible not only for the many infarctive phenomena but also for the haemolytic anaemia. *H. Lehmann*

Stock, A. E. **Splenic Infarction associated with High Altitude Flying and Sickle Cell Trait.** *Ann. Intern. Med.* 1956, Mar., v. 44, No. 3, 554–6.

"An additional case is presented of splenic infarction in a Negro with sickle cell trait, precipitated by high altitude flying in an unpressurized cabin. The sickle cell trait was definitely established by hemoglobin electrophoretic patterns. The patient was treated without splenectomy, even though abdominal exploration was performed. With increasing awareness of this syndrome, particularly with the demonstration of sickling, conservative therapy is feasible and successful. This patient confirms the recent suggestion of Motulsky that sickle cell trait can be affected by anoxemia producing hemolysis and splenic infarction."

Rotter, R., Luttgens, W. F., Peterson, W. L., Stock, A. E. & Motulsky, A. G. **Splenic Infarction in Sicklemia during Airplane Flight: Pathogenesis, Hemoglobin Analysis and Clinical Features of Six Cases.** *Ann. Intern. Med.* 1956, Feb., v. 44, No. 2, 257–70, 1 fig. [32 refs.]

"1. Splenic infarction precipitated by airplane flight was observed in five Negroes and one Puerto Rican soldier with sicklemia.

" 2. Hemoglobin analysis revealed three patients with sickle cell trait, two with sickle cell–hemoglobin C disease, and one with sickle cell–thalassemia disease (microdrepanocytosis).

" 3. It is suggested that the following factors play a rôle in precipitating this syndrome: (a) hypoxia; (b) amount of sickling (S) hemoglobin (more than 40% in all six cases); (c) peculiarities of the splenic circulation: slowing of blood flow in the pulp, and poor collateral blood supply between splenic arterial branches.

" 4. The following criteria for air travel of persons with sicklemia are suggested: (a) Individuals with sickle cell trait should not fly at high altitudes in unpressurized airplanes unless a source of oxygen is available. (b) Individuals with splenomegalic sickle cell anemia, sickle cell–thalassemia disease and sickle cell–hemoglobin C disease should not fly unless ground level air pressure can be maintained.

" 5. Nonsurgical symptomatic treatment of flight-induced splenic infarction appears sufficient for most cases. However, splenectomy may be required in selected instances.

" 6. The occurrence of splenic infarction in individuals with the sickle cell trait emphasizes that this common condition can no longer be considered entirely benign.

" 7. It is desirable that the Armed Forces institute a paper electrophoretic screening program for the detection of sicklemia among Negro and Puerto Rican military personnel on induction. Similar screening tests should be preformed on any Negroes who fly repeatedly."

[See this *Bulletin*, 1955, v. 52, 572.]

Bezon, A. A propos d'une éventuelle résistance des sicklémiques à l'endémie palustre à *Pl. falciparum*. [**The Possible Resistance to Endemic *P. falciparum* Malaria in Sicklers**] *Méd. Trop.* Marseilles. 1955, July–Aug., v. 15, No. 4, 423–7.

The author has examined 3 groups of Kabrese in different localities in Northern Togoland, and has compared the incidence of sickling with that of malaria. The first group consisted of 280 children between the ages of 1 and 12 years, the second and third were from two different schools and were between 5 and 10 years old. The parasites found were in 70–90 per cent. of the cases *P. falciparum*, sometimes associated with *P. vivax*, and rarely *P. malariae*. Malaria was holo-endemic, with some increased transmission in the rainy season, and the work was carried out at the end of that season. No anti-malarial drugs had been received by the pupils of either school for the last 5 months. Of 408 non-sickling children 160 (40 per cent.) showed malarial infection, and of 50 sicklers 16 (32 per cent.).

The author considers it to be significant that there was an inverse ratio between incidence of sickling in his 3 samples and the percentage of children infected with malaria: the incidences of sickling were as

follows: 8·2, 17·1 and 15·7 per cent.; and the number of sickling children infected with malaria were 9 of 21, 1 of 12, and 6 of 17 respectively. [As the area was holo-endemic, and the children above the age of 2 at least would be expected to be protected by acquired immunity—whether they were sicklers or non-sicklers—one is not surprised that there was no significant difference in the parasite rates.] *H. Lehmann*

MABAYOJE, J. O. **Sickle-Cell Anaemia. A Major Disease in West Africa.** *Brit. Med. J.* 1956, Jan. 28, 194–6, 2 figs. [16 refs.]

After reviewing recent literature relating to sickle-cell disease, the characteristics of which he describes, the author presents clinical and laboratory data relating to 13 patients. These patients had been selected from among 63 encountered in the General Hospital, Lagos, between April 1952 and March 1955. One of them presented at the age of 6 with aphasia which had developed during a sickle-cell crisis. In two of the patients joint disease caused by the sickle-cell abnormality had been confused with tuberculous arthritis. In two other patients megaloblastic change was found in the bone-marrow and was considered probably to be caused by an associated nutritional deficiency. In another patient a laparotomy had been carried out because of severe pain occurring during a sickle-cell crisis. No abnormalities had been found and it was at first thought that the operation had been needless. Three years later, however, he had a further severe crisis in which there was much abdominal pain and on this occasion gall stones were confirmed by cholecystography. The possibility of secondary causes of abdominal pain being present must never be overlooked in patients suffering from sickle-cell crises.

Reference is made to previously expressed views that sickle-cell anaemia is less common among Negroes in Africa than among those in America. This view is challenged and it is pointed out that the disease is common on the west coast of Africa, that as many as 5 patients with it have been present together in the medical wards of the General Hospital, Lagos, and that 3 new patients have walked into the medical out-patient department in the course of one morning clinic. No attempt has been made to relate numbers of patients with the disease encountered at this hospital to general population statistics, for as is rightly pointed out, only a misleading impression of its frequency would thus be obtained. The conclusion is reached, however, that sickle-cell anaemia is a major disease in West Africa. It is also suggested that there is an unknown protective factor that might explain why the disease is less common in parts of Africa than the incidence of the trait would suggest. [Until reliable statistics have demonstrated that the disease is less common in Africans than is to be expected, however, it appears premature to suggest the presence of such an unknown protective factor.] *A. W. Woodruff*

Scott, R. B., Ferguson, Angella D., Jenkins, M. E. & Clark, Harriette M. **Studies in Sickle-Cell Anemia. VIII. Further Observations on the Clinical Manifestations of Sickle-Cell Anemia in Children.** *Amer. J. Dis. Children.* 1955, Dec., v. 90, No. 6, Sect. 1, 682–91, 8 figs. [15 refs.]

This is a survey of 63 children with sickle-cell anaemia admitted to hospital on 401 different occasions from 1940 to 1954. The subjects were all Negro children seen in Washington D.C., and their ages varied from 3 months to 15 years. The older the children the fewer were the occasions when hospital treatment was required. Only 4 of the children died in hospital, one of bronchial distress and cerebral thrombosis, one in crisis with a haemoglobin level below 2 gm. per cent., one of convulsions associated with hyperpyrexia, and one from a transfusion reaction. There is a useful table summarizing the diseases and symptoms easily confused with sickle-cell anaemia, and a discussion of treatment. The most reliable therapy were blood transfusions and control of intercurrent infections.

[It will be of great interest to follow further reports by these authors. From 1954 they have employed electrophoresis to diagnose the various types of sickle-cell disease and so to differentiate, from now on, between the true (homozygous) sickle-cell anaemia and sickle-cell-haemoglobin C disease.] *H. Lehmann*

Mintz, A. A., Church, G. & Adams, E. D. **Relationship of Cholelithiasis to Sickle Cell Crises.** *Southern Med. J.* 1956, Mar., v. 49, No. 3, 205–9, 4 figs.

"Two cases of cholelithiasis in patients having sickle cell anemia have been presented.

"Twenty patients in the pediatric age group with sickle cell anemia were examined by oral cholecystograms to determine the incidence of detectable biliary calculi. This technic was responsible for the diagnosis of cholelithiasis in two patients in the group.

"A review of the literature with respect to biliary calculi in the Negro in general and specifically in sickle cell anemia has been included."

de Torregrosa, Mercedes V., Ortiz, A. & Vargas, D. **Sickle Cell-Spherocytosis associated with Hemolytic Anemia.** *Blood.* 1956, Mar., v. 11, No. 3, 260–65, 3 figs. [22 refs.]

"1. A case exhibiting the rare combination of sicklemia with spherocytosis has been presented and discussed.

"2. The importance of spherocytosis in producing the hemolytic anemia, as well as the harmless role played by the sickle cell trait is discussed. The beneficial effect of splenectomy confirmed this interpretation.

"3. Studies with paper electrophoresis revealed normal adult and fetal hemoglobin values in the father, brother and paternal grandmother. Sickle hemoglobin was present in the patient's and in the mother's blood."

WHEBY, M. S., THORUP, O. A. & LEAVELL, B. S. **Homozygous Hemoglobin C Disease in Siblings: Further Comment on Intraerythrocytic Crystals.** *Blood.* 1956, Mar., v. 11, No. 3, 266–72, 4 figs. [11 refs.]

"1. Two Negro brothers with homozygous hemoglobin C disease are reported. In one splenectomy was performed.

"2. Intraerythrocytic crystals in smears of peripheral blood were demonstrated only in the patient who had splenectomy. The crystals could not be found in re-examination of bone marrow preparations of this patient that were made prior to splenectomy.

"3. Absence of the spleen may be a necessary factor for the formation of these crystals.

"4. The presence of homozygous C disease is compatible with a normal life span."

LEHMANN, H. & MACKEY, J. P. **The Absence of Haemoglobin C in 104 East Africans living in Dar es Salaam.** *Man.* 1955, Dec., v. 55, Articles 197/207, 186.

The authors discuss the history and literature of haemoglobin C, with particular reference to Africa [this *Bulletin*, 1954, v. 51, 1188; 1955, v. 52, 290, 477, 572] from which it would seem that haemoglobin C is restricted to tropical West Africa and falls in incidence from west to east. In confirmation of the distribution so far as it is known, they have examined 104 random blood specimens from East Africans in Dar es Salaam, Tanganyika. In 12 of them haemoglobin S was found, but no haemoglobin C was discovered. The wide variety of tribes from which these persons came is shown on a list. *H. J. O'D. Burke-Gaffney*

BIRD, G. W. G. & LEHMANN, H. **The Finding of Haemoglobin D Disease in a Sikh.** *Man.* 1956, Jan., v. 55, Articles 1/22, 1–2, 5 figs. on pl. [10 refs.]

The authors, with MOURANT, have already recorded the finding of one Sikh soldier out of 109 examined who was heterozygous for the genes responsible for haemoglobin A and D [this *Bulletin*, 1955, v. 52, 1227].

They now record finding haemoglobin D alone in one of 62 further Sikh soldiers, and thus the phenotype DD was found for the first time. The technique of investigation is described and the findings illustrated.

The soldier was apparently healthy and no physical abnormalities were detected. However, his blood picture showed some unusual features, which are detailed. There was no evidence of undue haemolysis. The mean corpuscular haemoglobin was low, but the haemoglobin level of the blood was brought to near normal by an increase of red cell concentration. The blood smear is illustrated: the picture resembled that of haemoglobin E disease, and had the haemoglobin not been analysed, the condition might have been diagnosed as a compensated thalassaemia, though the findings were not quite typical. It is suggested that because of similar observations in the Punjab, it might be worth while to re-examine cases of thalassaemia reported from North-West India for abnormal haemoglobin.

The finding of 2 persons with haemoglobin D among 171 unrelated Sikhs suggests that this haemoglobin may be less uncommon than negative surveys in Africans, Europeans and North Americans would seem to suggest.

In a footnote it is added that 108 more Sikhs and 13 Punjabi Hindus are being examined: so far it seems that 3 more instances of AD have come to light in Sikhs and 1 in a Hindu. *H. J. O'D. Burke-Gaffney*

Jonxis, J. H. P., Huisman, T. H. J., van der Schaaf, P. C. & Prins, H. K. **Amino-Acid Composition of Haemoglobin E.** [Correspondence.] *Nature.* 1956, Mar. 31, v. 177, 627–8, 1 fig.

VENOMS AND ANTIVENENES

Peters, J. A. **Herpetological Type Localities in Ecuador.** *Rev. Ecuatoriana de Entom. y Parasit.* Guayaquil. 1954–1955, v. 2, Nos. 3/4, 335–52, 8 figs.

Lee, C. Y., Chang, C. C. & Kamijo, K. **Cholinesterase Inactivation by Snake Venoms.** *Biochem. J.* 1956, Apr., v. 62, No. 4, 582–8, 1 fig. [13 refs.]

Tange, Y. Beitrag zur Kenntnis der Morphologie des Giftapparates bei den japanischen Fischen. XIII. Über den Giftapparat bei *Liobagrus reinii* (Hilgendorf). [**Morphology of the Poison Apparatus of Japanese Fish. XIII. Poison Apparatus of** *Liobagrus reinii*] *Yokohama Med. Bull.* 1955, Aug., v. 6, No. 4, 255–65, 5 figs.

Loison, G. Poissons vénéneux du Pacifique Sud. [**Venomous Fish of the South Pacific**] *Rev. Méd. et d'Hyg. d'Outre-Mer.* 1956, Apr. 15, v. 28, No. 245, 66–72.

A general account.

TOXOPLASMOSIS

Tolentino, P. **Italian Contribution to the Study of Toxoplasmosis.** *Scientia Med. Italica.* 1955, Apr.–June, v. 3, No. 4, 711–30, 14 figs. (3 coloured). [53 refs.]

The author follows his previous publications on the general history of toxoplasmosis with a paper devoted to the contributions of Italian workers in this field of study.

He recalls, for example, the discovery of *Toxoplasma*, in rabbits, in Brazil by Splendore in 1908, the first description, by Carini, of spontaneous infections in the pigeon and guineapig, the first recorded case, by Mello, of canine toxoplasmosis, and the earliest report, by Sangiorgi, of *Toxoplasma* in the rat and mouse. The studies of numerous other Italian authors on the physiology and taxonomy of the parasite, and the chemotherapy of toxoplasmosis are briefly mentioned.

Most of the paper is devoted to clinical aspects of the disease. This is in the form of a discussion of previously published case reports by the author and other workers in Italy. Several cases of presumed and proved congenital toxoplasmosis are compared and there are good illustrations of cerebral calcifications and eye lesions. Some cases discussed have been fatal infections, and the parasites were isolated from cerebrospinal fluid; some were of the subacute type showing chorioretinitis, hydrocephalus, convulsions and cerebral calcifications; still others have been definitely chronic cases. Of the last type a case is quoted, from Ruosi, of a 23-year-old woman who had suffered from intermittent convulsions since the age of 2, and showed muscular hypertonia and mental deficiency but no chorioretinitis or cerebral calcifications. Toxoplasmas were isolated from cerebrospinal fluid. Radiological and eye examinations may reveal evidence of *Toxoplasma* infection in apparently healthy persons.

A woman rabbit-breeder (quoted from Scotti) apparently acquired an infection which was successfully treated by sulphonamide therapy. The successful treatment of anterior uveitis [due to toxoplasmosis?] with sulphonamide associated with aureomycin is mentioned. Human toxoplasmosis has been reported from almost every region of Italy, and a list of cases is given.

The neutralization test for *Toxoplasma* on the sera of 71 people suffering from " various nervous diseases with or without characteristic

signs of toxoplasmosis, and also on subjects affected by splenomegaly of uncertain aetiology" gave 18 per cent. positive results. This figure is considered high by the author, who suggests non-specific reactions as the reason [the age and other details of the subjects are not given here, but from other authors' findings this percentage does not seem unduly high].

Using the dye test the author distinguishes between recent infections (titres of 1 in 256 to 1 in 2048) and "remote" infections (1 in 16 to 1 in 64) in congenital forms with cerebral calcifications and chorioretinitis in subjects from 8 to 12 years old.

A larger percentage of positive human sera was found in surveys with the dye test than with the neutralization test [although the author has already suggested non-specific reactions with the neutralization test] and figures obtained compared favourably with the results using Frenkel's skin test. The skin test showed a rise in the percentage of positive results with increase in age. The author discounts the possibility that any positive results might be due to antigenically related organisms. [However, see this *Bulletin*, 1955, v. 52, 84.] The failure of antibodies to pass into the aqueous humour of chronically infected animals is discussed.

The Italian contributions to the study of the epidemiology and pathogenesis of *Toxoplasma* are given and the opinion is stated that mucous membranes may represent the most likely route of infection. Animals are readily infected by placing the parasites in the conjunctival sac, and on the vaginal and nasal mucous membranes.

Infection by the oral route is considered less probable by the author [many authors will disagree with this]; faeces and urine may contain viable parasites.

The factors associated with the pathogenicity of *Toxoplasma* may be the quantity of protozoa available, the state of conservation of the infective material, virulence of the strain, and the species and age of host. Concomitant infections and hormonal factors may play their part in the course of infection.

There is a useful list of references. *R. Lainson*

Pearson, H. A. **Congenital Toxoplasmosis.** *U.S. Armed Forces Med. J.* 1956, Feb., v. 7, No. 2, 278–84, 4 figs.

"A case illustrating the classical findings of congenital toxoplasmosis is presented. Chorioretinitis, internal hydrocephalus, and intracranial calcifications which are characteristic of this syndrome were present. It is suggested that congenital toxoplasmosis be included in the differential diagnosis when mental retardation, convulsions, blindness, hydrocephaly, or microcephaly are encountered. Fundoscopic examination for chorioretinitis and roentgenographic examination of the skull for intracranial calcifications offer the most satisfactory means of establishing the diagnosis."

Paul, J. & Schlanstedt, R. Antikörperbildung nach Toxoplasma-Antigenzufuhr bei Kindern. [**Development of Antibodies in Children after Introduction of *Toxoplasma* Antigen**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1956, Feb., v. 113, No. 1, 1–14, 1 fig. [40 refs.]

Sixty-one infants and children with negative dye tests for toxoplasmosis were inoculated intracutaneously, by mouth or by dropping antigen into wounds, the inoculum being Westphal's complement-fixing antigen. Two weeks later 51 (84 per cent.) had low titre dye test antibodies. As controls 43 children were inoculated intracutaneously with the fluid used to control the intradermal toxoplasmin test; in none did the dye test become positive. The significance of these findings is considered, with particular discussion of the fact that the Westphal antigen stimulates antibody formation, of the failure of 16 per cent. of the children to develop antibodies, and of the route by which the human being becomes infected. It appears that active immunization against toxoplasmosis along these lines is unlikely to be successful. *I. A. B. Cathie*

Potts, R. E. & Williams, A. A. **Acute Myocardial Toxoplasmosis.** *Lancet.* 1956, Apr. 21, 483–4.

"A case of acute myocardial toxoplasmosis from which the organism was isolated is described.

"It is suggested that the source of infection in this case was from a dog."

See also p. 932, Rawal, *et al.*, **Ocular Toxoplasmosis.**

DERMATOLOGY AND FUNGUS DISEASES

Converse, J. L. **Growth of Spherules of *Coccidioides immitis* in a Chemically Defined Liquid Medium.** *Proc. Soc. Exper. Biol. & Med.* 1955, Dec., v. 90, No. 3, 709–11, 2 figs.

In the present highly successful experiments for the development of the sporangial (parasitic) form of *Coccidioides immitis in vitro*, the author used the synthetic, liquid culture medium of Roessler *et al.* [*Bull. Hyg.*, 1947, v. 22, 160] supplemented by a trace of zinc sulphate; the original formula contains glucose, ammonium acetate, monopotassium and dipotassium phosphates and magnesium sulphate. For the inoculum, a particular strain of *C. immitis*, M 11, was grown in

this medium for 28 days at 34°C. with continuous mechanical shaking. For the actual experiment, a 5-fold dilution of the medium with water was used, and the inoculum was a suspension of approximately 10 millions of the viable arthrospores from the 28 days' culture. The experimental cultures were made in 250 ml. Erlenmeyer flasks containing 50 ml. of the diluted medium, and were incubated at 34°C. with continuous shaking. Samples of the culture were withdrawn at 24-hour intervals and examined microscopically in wet lactophenol blue mounts, and plate cultures were made to determine the amount of growth. There was an initial mycelial growth on which the "spherules" developed in terminal chains. These spherules, which were seen after 72 hours' incubation, were most numerous after 96 to 120 hours. They showed all the developmental stages of the parasitic form up to the mature sporangium filled with endospores. The sporangia measured up to 80 μ in diameter, and the endospores 1 to 5 μ.

After the 5th day, the cultures showed a tendency gradually to revert to the mycelial phase, which may be attributable to exhaustion of the nutrient, or accumulation of metabolic products. In this connexion, reference should be made to the technique of Lubarsky and Plunkett [this *Bulletin*, 1956, v. 53, 241] for replenishing the culture fluid during growth.

The experimental work described was done chiefly with the strain M 11, but similar although less striking results were obtained with 60 per cent. of 38 other strains. *J. T. Duncan*

Smith, C. E., Saito, Margaret T. & Simons, Susan A. **Pattern of 39,500 Serologic Tests in Coccidioidomycosis.** *J. Amer. Med. Ass.* 1956, Feb. 18, v. 160, No. 7, 546–52, 4 figs. [Refs. in footnotes.]

In an earlier report on the serological diagnosis of coccidioidomycosis, Smith *et al.* [this *Bulletin*, 1951, v. 48, 73] described methods of performing the precipitin and complement-fixation tests, and analysed the results of these tests on 21,000 samples of serum from cases of coccidioidomycosis. Since then an additional 18,500 samples of serum have been examined and the observations on these have, in all respects, confirmed those on the first group.

Specific precipitins appear in the blood at an early stage of the infection but they are transient and the precipitin test is of little value after the fifth month. The complement-fixing antibodies appear at a later date than the precipitins and are an indication of progressive infection, but even in clinically manifested primary pulmonary coccidioidomycosis the serological diagnosis in about one-third of the cases must rest entirely on the precipitin test. However, precipitins are rarely found in disseminated infections and are almost unknown in relation to coccidioidal pulmonary residuals, with or without cavitation.

The complement-fixing antibodies appear usually during the first 3 months and a few reversions may occur by the second month. The titre of complement-fixing antibody is generally a measure of the severity of the infection, and titres in excess of 1 in 16 or 1 in 32 usually indicate the probability of dissemination.

The presence of antibody in cerebrospinal fluid is an indication of coccidioidal meningitis, as these antibodies do not pass through the blood-brain barrier. They do, however, pass through the placenta from the maternal to the foetal circulation and they may persist in the blood of the infant for some months. Congenital coccidioidomycosis is, however, not known to occur. *J. T. Duncan*

Campins, H. Coccidioidomicosis pulmonar. [**Pulmonary Coccidioidomycosis**] *Rev. Sanidad y Asistencia Social.* Caracas. 1953, Jan.–Apr., v. 18, Nos. 1/2, 177–84.

Chick, E. W., Sutliff, W. D., Rakich, Jennie H. & Furcolow, M. L. **Epidemiological Aspects of Cases of Blastomycosis admitted to Memphis, Tennessee, Hospitals during the Period 1922–1954: a Review of 86 Cases.** *Amer. J. Med. Sci.* 1956, Mar., v. 231, No. 3, 253–62, 1 fig. [37 refs.]

A review of the clinical records of 86 patients with North American blastomycosis treated at 7 hospitals in Memphis, Tennessee, during the period 1922–1954, gave the following data, chiefly of epidemiological interest: in 52 patients (60·5 per cent.) the disease was of the disseminated type; in 23 patients (26·7 per cent.), of the cutaneous type, and in 11 (12·8 per cent.) there were only pulmonary lesions. *The age factor*: various ages from 5 to 71 years were represented, but 30 per cent. of the patients were in the age-group 26–35 years; below this group the numbers diminished sharply and above it more gradually. *The sex factor*: males predominated in the ratio of about 6·1 to 1 female. *The race factor*: coloured patients outnumbered white patients in the proportion of about 2 to 1, which is remarkable in view of the predominance of the white race in the general population of Tennessee where they outnumber the coloured race by more than 5 to 1. *The occupational factor*: the infection had no clear connexion with any particular occupation, but manual labourers and especially those engaged in agriculture or forestry seemed to be more prone to the disease than other workers.

The cases were sporadic and there were no stated meteorological, geographical or geological factors related to the infections, except that the illustrative map shows the presumed sites of infection to be chiefly in the neighbourhood of the Mississippi river. The data set out are

consonant with the findings of other observers, except in the matter of distribution in the two races, the disease usually being found more frequently in the white than in the Negro race. *J. T. Duncan*

Polo, F. J., Brass, K. & de Montemayor, L. Enfermedad de Gilchrist en Venezuela. Primer caso.—Estudio clínico.—Comprobación histológica. Aislamiento y determinación de la primera Cepa Suramericana de *Blastomyces dermatitidis* (45). [**North American Blastomycosis in Brazil; Isolation and Identification of the First South American Strain of** *Blastomyces dermatitidis*] *Rev. Sanidad y Asistencia Social.* Caracas. 1954, May–Aug., v. 19, Nos. 3/4, 217–35, 28 figs. on 9 pls. [49 refs.]

TROPICAL OPHTHALMOLOGY

Schaible, G. Zur Therapie des akuten Trachoms. [**Treatment of Acute Trachoma**] *Ztschr. f. Tropenmed. u. Parasit.* Stuttgart. 1956, v. 7, No. 1, 116–20, 1 fig. [12 refs.]

The English summary appended to the paper is as follows:—

"During a local outbreak of trachoma in a northern district of Sumatra, 167 juveniles and 7 babies were treated with instillations of chloromycetin in 0·5 to 1·0 solution three times daily, or with 1·0 percent aureomycin ointment. In the initial stages, conjunctival follicles were touched with 1·0 percent silver nitrate twice weekly and three to five times in all. 101 of 174 patients showed no more follicles after two weeks; 25 patients relapsed. Three months later 171 patients were clinically cured.

"The author believes that chloromycetin and silver nitrate combined form a practical and effective therapy for fresh trachoma. He dissuades rough mechanical squeezing of sprouting follicles because of the violent conjunctival reaction that often ensues."

Decour, M. Organisation de la lutte contre les maladies oculaires au Maroc. [**Organization of Control of Eye Diseases in Morocco**] *Maroc Méd.* 1955, Oct., v. 34, No. 365, 1225–38, 1 map & 5 charts. [Refs. in footnotes.]

See also p. 947, Brown, **Observations on the General Incidence of Blindness and certain other Diseases in Uganda.**

Rawal, B. D., Patel, R. J., Vakil, H. & Jhala, H. I. **Ocular Toxoplasmosis.** *Indian J. Med. Sci.* 1956, Jan., v. 10, No. 1, 55–8. [13 refs.]

" A case of ocular toxoplasmosis investigated by serological methods is described."

Weyts, E. J. **Ocular Manifestations in Onchocerciasis.** *Documenta Med. Geograph. et Trop.* Amsterdam. 1956, Mar., v. 8, No. 1, 29–38, 8 figs. [15 refs.]

This is a concise and accurate account of ocular onchocerciasis as experienced in the Belgian Congo (Léopoldville) but the description given of the disease would do equally well for any other locality where it occurs.

The author's findings are based upon the detailed study of 180 Congolese and 15 white patients with ocular complications. It is a very sound account of this interesting tropical eye disease and can be recommended to those interested in the subject. It is illustrated by some helpful photographs and drawings.

The main conclusions reached by the author are as follows:

" (1) Onchocerciasis causes anatomical and clinical lesions of the eye. In the anterior segment: lesions of the conjunctiva, cornea, retina and the ciliary body; in the posterior segment the chorioretina and the optic nerve suffer fundamental changes. These lesions have specific aspects.

" (2) Biomicroscopy of the anterior segment, biopsy of the conjunctiva and ophthalmoscopic examination of the ocular fundus are very useful in establishing the localisation of onchocercal lesions in the eye.

" (3) The ocular lesions depend on the presence of microfilariae, and on an allergic factor. The larvae may penetrate into the eye by way of the anterior or the posterior segment.

" (4) The best treatment scheme appears to be: (*a*) excision of the nodules, (*b*) a 15-day course of carbilazine or hetrazan, and (*c*) a course of antrypol." *D. P. Choyce*

MISCELLANEOUS DISEASES

Gelfand, M. **Porphyria in the Rhodesian African.** *Central African J. of Med.* 1955, Nov., v. 1, No. 6, 281–5, 4 figs.

Two cases of porphyria were seen at the Salisbury African Hospital, Southern Rhodesia. The first was an African male of 34, complaining

of blisters on the fingers and backs of the hands. He also noticed an increase of hair on the temporal and masseter areas of the face. On examination there was scarring on the hands and dystrophy of some of the finger nails. Porphyrins were found both chemically and spectroscopically in the urine. The second case was that of a male of 24 who complained of blistering on the hands and darkening of the skin of the face. His urine had been dark for several months and was found to contain porphyrins.

The condition as encountered in Rhodesia is characterized by blisters on the hands or less frequently the feet, face, or other parts of the body. The mucosa of the tongue, mouth or pharynx is occasionally affected. The number of blisters is very variable and they tend to occur in crops. On rupture large circular ulcers are formed resembling trophic or tropical ulcers. Darkening of the skin of the face is usual, the pigmentation being either diffuse or spotted. Dystrophy or complete loss of finger nails is not unusual. Abdominal symptoms and neurological or psychological changes are rare. There is often some rise in blood pressure but constitutional symptoms are generally few and the prognosis as regards life is good. In differential diagnosis Brazilian pemphigus, dermatomyositis with bullae, the Stevens-Johnson syndrome, epidermolysis bullosa and even leprosy should be considered. No treatment appears to prevent the formation of blisters. These patients should not be given barbiturates or sulphonal. *H. T. H. Wilson*

Chancey, R. L. & Gipson, B. F. **Ainhum.** *U.S. Armed Forces Med. J.* 1956, Jan., v. 7, No. 1, 101–4, 3 figs.

Report of a case.

PARASITOLOGY: GENERAL

Taylor, Angela E. R., Terry, R. J. & Godfrey, D. G. **The Action of some Trypanocidal and Antimalarial Compounds on *Babesia rodhaini* (Piroplasmidea).** *Brit. J. Pharmacol. & Chemotherapy.* 1956, Mar., v. 11, No. 1, 71–3. [12 refs.]

Beveridge, Elizabeth. **The Activity of Phenanthridine Compounds against *Babesia rodhaini* in Mice.** With a Note on some Clinical Trials by P. G. Hignett. *Ann. Trop. Med. & Parasit.* 1956, Mar., v. 50, No. 1, 85–91, 1 graph. [17 refs.]

Basnuevo, J. G., Profilaxis de las enfermedades parasitarias y tropicales mas frecuentes en Cuba. [**Prevention of the Commoner Parasitic and Tropical Diseases in Cuba**] *Rev. Kuba Med. Trop. y Parasit.* 1955, Jan.–June, v. 11, Nos. 1/6, 18–23.

ENTOMOLOGY AND INSECTICIDES: GENERAL ZOOLOGY

[Papers on the toxic effects of insecticides in man are abstracted in the *Bulletin of Hygiene* under the general heading of Occupational Hygiene and Toxicology.]

Packchanian, A. & Pinkerton, Mary. **Further Studies on the Effect of Simulated Altitude on Eight Additional Species of Arthropods.** *Texas Reports on Biol. & Med.* 1955, v. 13, No. 4, 865–81. [15 refs.]

"1. The following eight species of arthropods were subjected to simulated altitude conditions by exposing them in an altitude chamber equipped to produce low temperatures with corresponding reduced atmospheric pressures: *Amblyomma americanum*, *Anopheles quadrimaculatus*, *Apis mellifera*, *Drosophila melanogaster*, *Oncopeltus fasciatus*, *Rhodnius prolixus*, *Triatoma phyllosoma*, and *Xenopsylla cheopis*.

"2. Most of the species tested survived two hours of exposure to conditions corresponding to an altitude of 10,000 feet above sea level. All of the arthropods studied were killed within 15 minutes at conditions simulating an altitude of 30,000 feet. Exposures at simulated intermediate altitudes produced paralysis or death in all species. The increase in death rate varied directly with exposure time for a given altitude; or, with altitude, for a given exposure time.

"3. The altitude factor responsible for the detrimental effect on insects is low temperature and not reduced pressure.

"4. Microfilariae, herpetomonas, and trypanosomes in the intestines of infected insects were found to survive conditions of 30,000 feet altitude after exposure for periods ranging from 2 to 24 hours, although these conditions invariably killed insects within 15 minutes."

Beckel, W. E. **Maintenance of Adult Mosquito Tissue in a Tissue-Culture Medium.** [Correspondence.] *Nature.* 1956, Mar. 17, v. 177, 534–5.

This is a preliminary note on attempts to obtain growth in ovaries of mosquitoes (*Aëdes hexodontus*, *A. aegypti*, and *A. communis*). The ovaries were removed and suspended in a tissue-culture medium similar to that used for culture of monkey kidney in poliomyelitis vaccine research. There was migration of strands of tissue, and muscular contraction for 7 days (60 days for *A. aegypti*), but no ovarian development

nor sign of mitosis in final preparations. [See also this *Bulletin*, 1954, v. 51, 1229, and the Note relating to this paper, *ibid.*, 1955, v. 52, 437.]

D. S. Bertram

Haddow, A. J. **Rhythmic Biting Activity of certain East African Mosquitoes.** [Correspondence.] *Nature.* 1956, Mar. 17, v. 177, 531–2, 1 fig.

The author discusses the similarity in the peaks of activity he has observed for a mosquito *Tacniorhynchus fuscopennatus* and those for a caddis fly studied by others (*Nature*, 1955, v. 175, 1122). Both insects are particularly active and on the wing 20 to 40 minutes after sunset and again at similar times before sunrise. The work on these insects has been done at points within 65 miles of each other in Uganda. This timing in the biting cycle of the mosquito and in the flight rhythm of the caddis fly, together with other factors briefly set out, are thought to indicate that the important stimulus to their activity is a particular low level of light intensity. *D. S. Bertram*

O'Gower, A. K. **The Rate of Digestion of Human Blood by Certain Species of Mosquitoes.** *Australian J. Biol. Sci.* 1956, Feb., v. 9, No. 1, 125–9. [14 refs.]

The benzidine test, sensitive for minute amounts of iron porphyrins, was used as well as the precipitin test in determining the rate of digestion of human blood in *Aëdes aegypti*, *A. concolor*, *A. notoscriptus*, *A. scutellaris*, and *Culex fatigans* fed for the first time in the laboratory. They were kept at 27 ± 1°C. and at 2 ± mm. Hg saturation deficiency after the meal and sample specimens were smeared on filter paper at 4-hour intervals for testing. For the initial 36 to 40 hours some batches of mosquitoes were kept in different light conditions varying from constant darkness to constant light, through light-to-darkness ratios of 2 to 1, 1 to 1, and 1 to 2.

When light and dark periods were equal *A. scutellaris* digested most rapidly (31 hours), *A. concolor* most slowly (48 hours), and the others at intermediate rates. The rates are expressed as hours required for 50 per cent. of a batch to have completed digestion. Increased darkness increased the rate of digestion in *A. notoscriptus*. Mosquitoes 3 weeks old digested as rapidly as those 1 week old. *D. S. Bertram*

Harant, H., Attisso, M. & Rioux, J. A. Sur l'écologie des Diptères Culicides. III. Les espèces limnodendrophiles et leur biotope. [**Ecology of Mosquitoes. III. Species Inhabiting Ponds and Trees and their Biotype**] *C.R. Soc. Biol.* 1955, Aug.–Sept., v. 149, Nos. 15/16 & 17/18, 1626–31.

Blazquez, J. & Maier, J. Ginandromorfismo en *Culex fatigans* sometidos por generaciones sucesivas a exposiciones de DDT. [**Gynandromorphism in *Culex fatigans* exposed to DDT for Successive Generations**] *Rev. Sanidad y Asistencia Social.* Caracas. 1951, Sept.–Dec., v. 16, Nos. 5/6, 607–12, 2 figs. on 2 pls. [13 refs.]

Haines, T. W. **Breeding Media of Common Flies. II. In Rural Areas.** *Amer. J. Trop. Med. & Hyg.* 1955, Nov., v. 4, No. 6, 1125–30.

Collections of breeding materials were made in 3 rural towns (average population 1,000) in South-West Georgia about 15 miles apart. Cows, pigs and chickens were kept by the inhabitants and less than one-half of the dwellings were connected to sewage disposal systems. *Musca domestica* was found breeding in 19 out of 20 types of breeding habitat classified under animal-pen litter (manure), animal carcasses, animal excrement, fruit and vegetable waste, and miscellaneous. It was not bred from fish remains. Animal-pen litter (excrement plus straw and animal food) was the commonest breeding habitat; 87 per cent. of the house-flies were bred from animal refuse (litter, excrement and carcasses), a result similar to previous records from urban areas [this *Bulletin*, 1954, v. 51, 437]. During intervals of dry weather, soil and garbage soaked with dish water and washing water became breeding foci. Other flies (*Stomoxys*, *Phaenicia*, *Sarcophaga*, *Muscina*, *Ophyra*, *Hydrotaea*, *Calliroga*, *Limnophora*, *Calliphora* and *Phormia*) did not breed in so wide a variety of habitats. The distribution of the flies in the breeding materials is set out in detail in 5 tables. *B. R. Laurence*

Schoof, H. F. **Survey and Appraisal Methods for Community Fly Control Programs.** *Pub. Health Service Publication No. 443. Pub. Health Monograph No. 33.* Wash. 1955, Nov., pp. iv + 18, 10 figs. [19 refs.]

In the past decade the technique of measuring house-fly populations in urban areas has been intensively developed with the use of the Scudder grill as a standard sampling device. This critical review considers the merits of the method and compares it with the older usage of fly-traps, and with reconnaissance which is a modification of the grill technique. It is concluded that use of the grill, or reconnaissance, provides the best available means of obtaining measures of fly abundance which are sufficiently standard and reliable to allow comparison of data over a period of time and from different places. Considerable space is given to describing the application of a Scudder grill survey, or reconnaissance, to a city. A plea is put forward for more attention of this kind in measuring the effect of fly control schemes. Fly-traps have some advantages over the grill when data are required on different species of

fly and blowfly in an area, although an experienced person is able, with a grill, to record data for 9 different kinds of fly. *D. S. Bertram*

Hansens, E. J. **Control of House Flies in Dairy Barns with special reference to Diazinon.** *J. Econom. Entom.* 1956, Feb., v. 49, No. 1, 27–32.

"Tests of phosphate insecticides for house fly control were continued in New Jersey using both residual treatments and wet and dry baits. Diazinon was by far the best material tested. Other materials in order of effectiveness were: Dow ET-14 (O,O-dimethyl O-2,4,5-trichlorophenyl phosphorothioate), Am. Cyanamid 4124, Chlorthion, Dow ET-15 (O-methyl O-2,4,5-trichlorophenyl phosphoramidothioate) and malathion. Of the dry baits, Diazinon and Bayer L 13/59 were best. Dow ET-14, Dow ET-15, Am. Cyanamid 4124, and certain malathion formulations were also effective. Wet baits were about equal to dry baits but had the advantage of some residual action. The 'plate' method of testing baits was found to be unsatisfactory for bait evaluation. Use of residual sprays supplemented by baits when the residual started to fail gave poorer fly control than additional residual treatments. Baits were not as effective as residual applications and failed to control biting flies.

"Analysis of milk from herds housed in barns sprayed with Diazinon or treated with Diazinon baits showed that there was no Diazinon in the milk, no cholinesterase inhibitor, and no effect on flavor.

"Horn flies were controlled for upwards of 2 months on herds housed in barns sprayed with Diazinon even though animals were only brought into barns for feeding and milking. Tests with house flies in sprayed barns and on unpainted plywood panels in the laboratory showed that flies are killed in part by fumigation and in part by direct contact with Diazinon. Also flies may be killed when they contact unsprayed surfaces on which Diazinon may deposit by transfer from sprayed surfaces."

Johnson, W. T., Langford, G. S. & Lall, B. S. **Tests with Organic Phosphorus Insecticides for Fly Control.** *J. Econom. Entom.* 1956, Feb., v. 49, No. 1, 77–80.

Parrot, L. & Doury, P. Notes sur les Phlébotomes. LXVIII.—Nouveaux Phlébotomes du Hoggar. [**Notes on** *Phlebotomus, LXVIII*: **New** *Phlebotomus* **Species in Hoggar**] *Arch. Inst. Pasteur d'Algérie.* 1955, Dec., v. 33, No. 4, 315–21, 4 figs.

Prívora, M. & Samšinák, K. Příspěvek k poznání ektoparasitů hlodavců v Čechách. [**Contribution to the Knowledge of Ectoparasites of Rodents in Bohemia (Czechoslovakia)**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1956, v. 5, No. 1, 34–6. [10 refs.] English summary (5 lines).

Forgash, A. J. **Differences in Arsenic Tolerance among the Sexes and various Stages of the American Cockroach.** *J. Econom. Entom.* 1956, Feb., v. 49, No. 1, 39–43, 2 figs.

Cochran, D. G. **The Distribution and Metabolism of DDT injected into the American Cockroach.** *J. Econom. Entom.* 1956, Feb., v. 49, No. 1, 43–9. [22 refs.]

Grayson, J. M., Jarvis, F. E., Jr. & Levitan, M. **Transmission of Resistance to Chlordane in the German Cockroach.** *J. Econom. Entom.* 1956, Feb., v. 49, No. 1, 130–31, 1 fig.

Thornton, D. G. & Davis, J. M. **A Method of Sampling for the Drop Size of Aerial Spray Deposits.** *J. Econom. Entom.* 1956, Feb., v. 49, No. 1, 80–83.

LABORATORY PROCEDURES

Evans, A. J. **Value of the Kahn Test in Africans.** *Brit. J. Venereal Dis.* 1955, Dec., v. 31, No. 4, 210–27, 1 fig. [Numerous refs.]

This long and well documented article (there are no less than 111 references) should be read in the original by all who are interested; it is impossible to include all the figures and deductions from them in an abstract. The first part is devoted to a survey of the literature, the definition of a biological false positive reaction (BFP), the value of different serological tests for syphilis (STS), the value of special antigens, the advantages of using several tests, and the treponemal immobilization test (TPI); technical false reactions (which can be excluded by repeated tests), the strength and the duration of BFP reactions are also discussed, and it is estimated that the reported incidence of these varies from 4 to 46 per cent.

The present investigation included the standard Kahn test on 6,797

adult African patients attending clinics in part of Northern Rhodesia; of these 6,006 were able to be followed and reported on.

The results were: positive 1,702, weak positive 1,239 and negative 3,065 [the proportion showing weak positive seems unduly large]. Assessment of results was made on history, scars, parents of a congenital syphilitic, partner's condition, history of repeated abortions, etc., and " other "factors.

An analysis of 1,889 cases giving positive or weak positive results gave the following results: probable true positives 1,220, possible true positives 338, possible BFP 160 and probable BFP 171; the true incidence of BFP results is estimated to be between 2·8 and 5·5 per cent. These last figures are higher than those from temperate climates and may be due (in part at least) to malaria and leprosy; of 137 malaria patients 38 (27·7 per cent.) gave positive Kahn reactions, the figures being higher in children than in adults; of 477 tests on patients with leprosy 18·4 per cent. gave positive results, the incidence being highest in lepromatous cases; surprisingly, positive reactions were twice as common in females as in males.

It is concluded that BFP reactions are due not to a single factor but to a multiplicity of different factors and a plea is made that a positive STS in a patient in the tropics should be followed by just as careful an investigation as it is in temperate zones. *T. E. Osmond*

See also p. 866, Gall, *et al.*, **The Estimation of Cerebrospinal-Fluid Protein in Sleeping Sickness: Sicard and Cantaloube's Method and a Sulphosalicylic-Acid Method.**

Bami, H. L. & Nair, C. P. **Composition of J.S.B. Stain and Factors affecting its Quality.** *Stain Technology.* 1955, Nov., v. 30, No. 6, 261–8, 3 graphs. [11 refs.]

REPORTS AND SURVEYS

Uganda. **Report of the Committee appointed by His Excellency the Governor to examine Medical and Health Services in Uganda** [Frazer, A. C., Chairman]. 1955, Dec., pp. xiv + 177, 1 graph & 4 separate folding maps (1 coloured). 1956. Entebbe: Govt. Printer, P.O. Box 33, Uganda. [Shs. 7.]

There having been some criticism of the medical services in Uganda, the Governor appointed a Committee to examine the present stage of development of medical and health services in the Protectorate and,

having regard to available resources of man-power and finances, to make recommendations for future policy. The Committee which, besides its Chairman, included 3 medical members and 4 others, spent 3 months on its task, holding no less than 259 meetings as well as undertaking a great deal of travelling and visiting all institutions of importance. It reviews the country and its people and then, first, the medical organization. This comes under a Ministry of Social Services under which it is administered by a Director operating through provincial and district medical officers. In parallel to it there are many institutions operated by missions, but without much mutual integration, and there are 92 private practitioners concentrated for the most part in 2 towns. The ultimate formation of a Ministry of Health and African Housing, an increase in the utilization of provincial medical officers, and public recognition of mission efforts with grants in aid subject to suitable control, are recommended. Neither Government nor mission institutions are distributed with a proper respect for the needs of the entire country and the formation of a central planning committee to ensure more uniform development is advised.

There is little knowledge of the nature of the problems to be met in Uganda, largely owing to the absence of any appropriate vital statistics; their universal collection and their correction by sample surveys are recommended. Each item of Government activity is considered. Health education is inadequate and too communal; it should be developed with more emphasis on personal aspects. Public health measures require improvement—by better food and drugs legislation, by the improvement of African housing, by the enlargement of both rural and urban health staff, by the dissemination of water supplies, and by the provision of less antiquated sewage systems in towns. Maternity work should be increased and accompanied by more care for the child.

Government hospitals and peripheral institutions suffer mainly from inadequacy of staff and the unsuitable training of some lower grades, and from a lack of supervision and constructive helpful control. This leads to a study of man-power problems in which it is advised that the medical establishment should be increased from 144 to 198 with comparable increases in nursing, auxiliary and senior lay staff. There is also a review of the training given in Uganda to nurses and auxiliaries, and this leads to constructive suggestions for modification to increase their efficiency at work. Man-power turns, however, not only on numbers available but on the suitability of conditions, and strong criticism is directed against housing provision for both African and European staff, its inadequacy probably being a large reason for present shortcomings. Salaries are on the whole adequate but the repeated statement that the Medical Officer (E.A.) is on a salary which is adequate, though his present salary scale is inappropriate, may be comprehensible in Uganda but not elsewhere. Considerable emphasis is laid on the further training of African graduates and it is hoped, by suitable modifications in Makerere,

that the intake of medical students in 1960 might approach 20. There are detailed comments on a number of other subjects, specialist and special services, private practitioners, medical equipment and drugs, pathological and medico-legal work and the effects of devolution on medical and health policy, which will be read with interest in Uganda but are mainly of local concern.

The report closes with a statement of the financial implications of the recommendations, which would lead to the medical budget absorbing 11·3 per cent. of the total revenue in place of the present 7·6 per cent., and a final recommendation that a charge of a shilling should be made for each entry to a medical unit (thus ending the present policy of free treatment) except for the indigent and some special groups.

[Despite the generally comprehensive nature of the report the reader is left wondering. The reviewer found no reference to a medical officer of health, an epidemiologist, a person with any special experience or knowledge of malaria, trypanosomiasis or schistosomiasis. Malaria control disappears in a few lines as too difficult. Schistosomiasis, fortunately, is often not a serious disability. The report, if acted on, will improve the present medical services by correction of faults, but it will not be remembered for any proposals on principle.]

G. Macdonald

Congo Belge. Fonds Reine Elisabeth pour l'assistance médicale aux indigènes du Congo Belge. Rapport sur l'Activité durant l'année 1953. [André, J., Médecin-Directeur-Adjoint du Fonds en Afrique.] [**Report of the Activities of Foréami during 1953**] 213 pp., 54 figs. on 24 pls., 2 folding maps & 7 diagrams. [1955.] Brussels: 14, Square de Meeûs.

Foreami started work in the relatively well developed Lower Congo, but in 1934 transferred its activities to the most backward area of the Congo, Kwango. The report opens with vivid accounts of the primitive nature of the country and the extreme difficulties encountered in starting work, which was then interrupted by the war. Movement to such a primitive area had been premature. In 1948 an integrated plan of development was brought into being and the present report describes its condition at the end of 5 years of operation. It is concluded that experimental work must continue for some years more before it can be replaced by routine operation. The principles of integration of medical, social, agricultural and economic advancement, a combination of field and institutional practice, and the provision of an adequate laboratory and hospital background hold good. The programme was advanced during the year by the opening of a nutrition laboratory at Feshi and the deployment of a radiographic unit for the diagnosis of tuberculosis and the provision of a treatment centre for cases found.

Work followed a pattern described in previous reports. Trypanosomiasis continues to decrease, new cases numbering 0·07 per cent. of the

population; the main method of control is pentamidine prophylaxis which has been very successful though the disease is not completely conquered. The history of the disease in this area is reviewed by Burke. Malaria control is chiefly by chemoprophylaxis to infants and schoolchildren, chloroquine having been the main drug used in the past. There have now been extensive trials of Daraprim [pyrimethamine], one in a dose of 12·5 mgm. every 2 weeks to schoolchildren, and another described in detail by Delauney and Hugon with standard doses once a month to rural populations. The marked decline in the spleen and parasite rates is described in detail, and it is concluded that Daraprim is superior to chloroquine as a medicament under these conditions. Increasing numbers of people with leprosy are attracted by the success of new treatments: the chief drug used is dapsone (DDS) and an analytical statement is given of the results of treatment by this and by allied drugs. The radiographic unit has revealed active tuberculosis in 8·6 per 1,000 of the people examined, a figure higher than in other parts of the Congo. The results of Mantoux survey are also given and show a steady rise from 15·4 per cent. in the 0–4 age-group to 70·9 per cent. in the 20–24 age-group. BCG vaccine was given to 237 people. Details are given of maternity and child welfare work and of the campaigns against yaws, syphilis and a number of other diseases.

A lengthy and fully documented section concerns demography and vital statistics, giving, among other things, death rates by serial age-groups from birth to old age, probably the only reliable data on this subject among any large group of people in such an under-developed area.

G. Macdonald

East Africa High Commission. **East African Tsetse and Trypanosomiasis Research and Reclamation Organization. Annual Report 1954–55** [Ford, J., Director]. 62 pp., 4 figs. on 2 pls. & 1 folding map. [22 refs.] [1955.] Nairobi.

In his introduction the Director notes certain proposals for reorganization which include the removal of the headquarters of the organization from Nairobi to Tororo (Uganda) where the Central Trypanosomiasis Research Laboratory is situated, and the formation of an advisory committee of the heads of territorial departments interested; the title of the organization is to be shortened to " The East African Trypanosomiasis Research Organization ". [These changes have been implemented.]

He then reviews certain developments in the trypanosomiasis situation, pointing out that tsetse can now be eradicated at a cost equivalent to that required for the common agricultural pests (*i.e.*, from under 1s. to about 20s. per acre). In discussing the slowness of progress in elimination of the fly he points out that of the 640,000 square miles of East Africa over 280,000 are infested by tsetse and that a zone 10–30 miles wide, conservatively estimated as of nearly equal area, lies under

threat, domestic animals kept there being subject to infection from trypanosomes; he puts the *net* amount regained from tsetse during the last 25 years at about 3 per cent. of the area actually infested. He notes that a large part of the anti-tsetse expenditure is needed to prevent deterioration of the present position, a big task on a front estimated at some 20,000 miles; an improvement in this position is reported from Tanganyika where, during the last 3 years of the 5-year period 1950–54 only 23 per cent. of the total expenditure was used in such defensive measures, as against 88 per cent. in the first 2 years. He then makes a point which has not so far been fully recognized, that the cost of reclaiming land from tsetse has been so much reduced now as to be considerably less than the cost of developing such land and of maintaining it in such a state that it cannot be re-infested, which is, in fact, the factor which now limits the amount of land that can be treated. He concludes that no speedy and wholesale elimination of fly by purely anti-tsetse measures is to be expected in the near future, but that, provided the East African economy continues to expand, a steady but slow decrease in the total area infested will result. It follows from this that the main practical problems to be solved lie in the contact zones between the tsetse-infested bush and the occupied lands, and he discusses how the research of his organization may be expected to contribute to the solution of these problems. [This important review of the situation should be read in the original by those interested, as it is impossible to give an adequate account of its details in this abstract.]

He then proceeds to the customary directorial review, much curtailed, of the work of the organization during the period under consideration, the 18 months between January 1, 1954 and June 30, 1955, instead of the usual 12 months; this is followed by detailed accounts of the work under Tsetse Research, Trypanosomiasis Research and Experimental Reclamation. [Again, these reports, which are themselves only summaries, should be consulted in the original, for here it is only possible to give an incomplete outline of their contents.]

The section on Tsetse Research was written by the late Dr. C. H. N. Jackson, whose death last year was a great blow not only to his own organization but also to tsetse work in general, and even to the wider study of animal ecology; a whole-page obituary pays tribute to his achievements. His account includes a note on the general plan of the work, recording the opening of two out-stations, the development of important studies on tsetse physiology, and of the techniques for the identification of the blood meals of tsetse, now producing reliable, if unexpected, results. Thus *G. morsitans* has been shown to be obtaining half their meals from wild pigs, mainly wart-hogs, in 3 areas in Tanganyika and 1 in Southern Rhodesia [see also this *Bulletin*, 1956, v. 53, 416, and Lovemore, above p. 865]; in contrast, a smaller sample of *G. pallidipes* (71 flies) showed over 60 per cent. of their feeds to have been on bush-buck, pigs providing only 11 per cent. The long-term cycle

of tsetse numbers continues to receive attention and its study is to be extended to include other tsetse species and other tsetse belts. New observations on the pupal sites of *G. morsitans*, *G. swynnertoni* and *G. pallidipes* are reported.

The section on Trypanosomiasis Research was written by Dr. K. C. Willett. He summarizes the results of the review by Dr. Fairbairn and himself of the main Tinde experiment on the infectivity to man of *Trypanosoma rhodesiense* transmitted through animals by fly [*ibid.*, 1956, v. 53, 550]. He also reports on some observations on the early stages of *T. rhodesiense* and *T. brucei* (both strains transmissible by fly) in the vertebrate host, the results of work carried out in collaboration with Professor R. M. Gordon; these show a marked difference in behaviour of the trypanosome in human beings and in susceptible animals. Certain strains of trypanosomes from South Africa, whose infectivity to man was in doubt, have been examined and found to be infective. Tests of Antrypol, submitted by the Tanganyika sleeping sickness specialist as suspect of being ineffective, suggested that it is important to use Antrypol solutions immediately after their preparation, as they seem to become ineffective on standing. Strains of trypanosomes from a sleeping sickness area in Uganda on the edge of the area depopulated by the great sleeping sickness epidemic of the beginning of this century (generally regarded as due to *T. gambiense*) and subjected during the early '40's to an acute outbreak of Rhodesian sleeping sickness, were found again to be of the *T. rhodesiense* type; 2 of these proved highly resistant to pentamidine but all were normally sensitive to Antrypol. A strain of human trypanosomes from the Central Nyanza district of Kenya, where the disease has always been of the *gambiense* type, were shown now to be of the *rhodesiense* type, though less virulent than typical strains. Reference was made to plans for an investigation of the vectors of human sleeping sickness in the Central Nyanza district of Kenya which will include a comparison of strains isolated from both *G. palpalis* and *G. pallidipes*. Tests of the efficiency of ethidium bromide against fly-transmissible *T. rhodesiense* showed this drug to be ineffective, in contrast to results obtained by Woolfe [*ibid.*, 1953, v. 50, 395] with a syringe-passaged strain, thus showing again the differences in drug response between such and freshly isolated strains.

Under the heading Cattle Trypanosomiasis further work is reported on acquired resistance to natural infections of *T. congolense* and mixed *T. congolense* and *vivax* by use of Antrycide pro-salt, a break through being ascribed to possible under-dosage occasioned by unsuspected increases in weight of the beasts under treatment; further observations are projected. The experiment on the transmission of *T. congolense* by vectors other than tsetse has been concluded and reported on in published papers by Lucas and Soltys; in two tests, with different strains of the trypanosome, cattle in kraals to which infected animals had been introduced became infected after intervals varying between 14 and 211 days, whereas none

of the control animals showed any infection; thus "mechanical" transmission of trypanosomiasis, previously demonstrated with certainty only under laboratory conditions, has now been shown to take place under field conditions, and there can no longer be any doubt as to its possibility in nature.

Some preliminary studies on the antigenic relationship between monomorphic and polymorphic trypanosomes by the neutralization test are noted as well as preliminary results suggesting that complement-fixing and neutralizing antibodies appear in the blood of sheep infected with *T. congolense* 7–10 days after infection. Preliminary results of attempts to culture *T. brucei* and *T. rhodesiense* in artificial media are reported as encouraging. An investigation is described relating the infection rates in nature of *G. pallidipes* and *G. palpalis fuscipes* to season, to habitat and to the darkness and paleness of the tsetse [which are supposed to depend on the humidity to which the pupae have been subjected].

The section on Experimental Reclamation [unsigned and therefore presumably written by Mr. Ford, though he quotes freely from the reports of the workers responsible] describes the progress of the pilot schemes on which all work [by the organization] is expected to finish during the following 12 months. It is interesting to note that in the Mkata Pilot Scheme (Tanganyika) mechanical clearing has been found useful, and that it has been possible to fell certain hardwood trees with mechanical saws, worked by a team of men, in 80–100 seconds, which would have taken a single axe-man up to an hour to fell. In contrast, an attempt to eradicate *G. brevipalpis* from riverine forest by the use of a Todd insecticide fog applicator proved unsuccessful, the weather conditions suitable to its use being of too limited duration. The Masai Pilot Scheme (Kenya) is reported as having been closed down, but it is expected to be replaced by a more suitable one, to be carried out by the Kenya Government. Satisfactory progress is reported in the Lambwe Valley Scheme (Kenya) which has now passed under the control of the Tsetse and Trypanosomiasis Survey and Control Unit of the Kenya Veterinary Department, although tsetse observations in the settlement areas are still, for the time being, carried out by the organization, which has also continued long-term observations on the fly (*G. pallidipes*) in the neighbourhood. Full details are given of the work accomplished in the Ankole Pilot Scheme (Uganda); this is an extensive scheme of discriminative clearing against *G. morsitans*, and details are also given of similar operations against the same tsetse in Urambo and in the Songea district, both in Tanganyika (the first was undertaken for the protection of the farming areas of the Overseas Food Corporation—now the Tanganyika Agricultural Corporation—against sleeping sickness). In North Ankole 310 square miles have been dealt with by the clearing of 6 per cent. of the area, while in Urambo clearing of the same percentage has so reduced the flies in the 22 square miles involved that whereas there were 29 cases of sleeping sickness in 1954 (14 of which occurred during the first 5 months) there were only 5 in

1955 up to May (all in one month, March); a trypanosomiasis rate of 7·2 per cent. per month in an experimental herd of cattle was reduced to 0·9 per cent. per month, and now a herd 200 strong is maintained. This method of control requires 18 months for the extermination of *G. morsitans*. Advice has been given on operations against *G. austeni* in Zanzibar and against *G. morsitans* in Songea (Southern Tanganyika). A list of memoranda and maps circulated among the territories is given. Four photographs illustrate certain aspects of the work of the organization —a refreshing change from those showing the buildings in which the work is carried out; two show the participation of Africans in the work. An interesting sketch map drives home the extent of the tsetse problem in East Africa and puts in perspective the activities both of the organization and of the Territorial Tsetse departments. A list of publications shows 17 papers published during the period under review, and 4 more were accepted for publication. [Earlier annual reports are reviewed in this *Bulletin*, 1954, v. 51, 1207; 1953, v. 50, 389, 1018.] *W. H. Potts*

VAN DER HOEVEN, Jan Arie. Resultaten van een onderzoek naar voeding en deficientie-verschijnselen bij autochthone zuigelingen in Nederlands Nieuw-Guinea. [**Results of a Nutritional and Medical Survey of Autochthonous Infants in Dutch New Guinea**] [Thesis]. 152 pp., 56 graphs, 1 map, 5 text figs. & 45 figs. on 11 pls. English summary. 1956. Brielle: Roopmansstraat 6, Holland.

This long thesis, written in Dutch, gives in great detail the results of a survey of the health and development of infants in New Guinea. The principal conclusion is that these infants were too short, too light and anaemic at birth and about the 4th to the 6th month. These defects are ascribed to intra-uterine deficiencies in the first place, to which is added protein deficiency in the food, especially in breast-milk.

The presence of enlarged livers in the first month of life was much commoner in areas where malaria was endemic. The adverse effect of malaria was less marked where nutritional conditions were satisfactory. Comparisons are made between the conditions in mothers and infants in coastal areas where sago is the principal food and those areas where tubers are largely consumed: in the latter regions nutrition and lactation are better and deficiencies existing at birth may be made up more effectively.

The importance of taboos is stressed: those relating to nutrition are nearly all concerned with protein. *viz.* they forbid the use of fish in the first year and meat in the first 2 years.

"In general, additional food is supplied too late; moreover, both the quality and quantity are insufficient."

Control of the high infant mortality must begin with improvement of the physical status of the mothers during pregnancy and the supply of

food rich in protein and vitamins for the infants during the early months of life. There are 45 informative photographs.

[This useful survey might with advantage be read with that of WELBOURN in Uganda, this *Bulletin*, 1956, v. 53, 478.]

H. J. O'D. Burke-Gaffney

BROWN, J. A. K. **Observations on the General Incidence of Blindness and certain other Diseases in Uganda.** *East African Med. J.* 1956, Jan., v. 33, No. 1, 19–24, 1 map.

This study originated in a leprosy survey in Uganda between 1952–1954, in which each person in a prescribed area selected at random was examined. Later the scope was widened and other conditions were noted. During the period 41 surveys were made and their distribution is shown on a map of Uganda.

In all, 55,947 persons were examined and 959 cases of leprosy were discovered, an incidence of 1·7 per cent. (range 0 to 4·1 per cent.). The epidemiological inferences are being published separately. A table, covering 30 surveys which included 23,016 persons, shows the incidence of blindness. Complete blindness was seen in 84 persons (0·36 per cent.) mostly adults. Four of the blind persons had leprosy and these constituted about 1 per cent. of the 386 persons with leprosy in this series.

The standard of nutrition in general was good and this is commented upon. A second table shows the results of 23 surveys including 17,042 persons in respect of the incidence of tropical ulcer, kwashiorkor, elephantiasis, inguinal hernia and hydrocele, which amounted respectively to 66, 35, 12, 220 and 175.

The author points to the varying standards of different observers in the diagnosis of mild kwashiorkor, but the figures do suggest that there was some geographical distribution: for example, there were 12 cases reported in one district and from 1 to 6 in others, while in 12 other areas no cases were recorded.

H. J. O'D. Burke-Gaffney

BOOK REVIEWS

RUSSELL, Paul F. [M.D., M.P.H.] **Man's Mastery of Malaria.** pp. xv + 308, numerous illustrations. 1955. New York: Toronto: London: Geoffrey Cumberlege, Oxford University Press, Amen House, Warwick Square, E.C.4. [25s.]

It has been said that history offers a measure for the just and well founded criticism of the doings of one's own time, and sets before the observer a mirror in which to compare the past and present in order to

draw therefrom well grounded conclusions for the future. It is on this text that Paul Russell writes his monograph on the mastery of malaria, leading up on every aspect through an account of happenings from ancient times to the present, and looking as far as possible into the future. He reviews successively the unfolding of the aetiology of malaria, malaria therapy, malaria prophylaxis in the wide sense of prevention by all means, international aspects of malaria, and the impact of malaria and its control on society.

The section on malaria aetiology starts with a statement of old speculations but leads up quickly to an examination of the mosquito theory including a detailed account of a Ceylonese document 1,400 years old, previously unknown to the reviewer, and thence to the tale of the detection of the parasites responsible and the means by which they are transmitted. This covers ground which has been highly controversial but which is here reviewed in a just and analytical manner which should set controversy at an end. In particular, the description of the parts played by Ross, Manson, Grassi, Bastianelli and Bignami in demonstrating transmission by anopheline mosquitoes is factual, complete and fair to all. The story continues up to the present day with an equally factual and objective review of the part played by different workers in the demonstration of the exo-erythrocytic forms of the malaria parasite. The section on the unravelling of malaria therapy is notable for its complete account of the history of cinchona, some of which has been discovered by the author himself and which differs considerably from the accepted legend.

The story of prevention gives less room for historical research but is one which the author has himself done much to develop, and on which he speaks up to the present minute in an authoritative and constructive manner. Preventive measures are now much fostered by international agencies which the author describes, concluding that the field is a unique one for international cooperation, but that the mere donation of material or imposition of schemes from outside without the constructive and general building of a public health department might be wasteful. The contribution on the impact of malaria on society is thoughtful and philosophical, dealing largely with the recent controversies on the influence of public health programmes, and particularly malaria control, on population density. Russell holds emphatically that it is the duty of the physician to save life in all circumstances and without reservation, the deliberate withholding of help for some hypothetical future good being unforgivable, while man's restaint of death can with proper forethought be matched by a regulation of birth.

The book displays from first to last a profound erudition and great broadness of view. Though not annotated, it is completed with a representative bibliography covering 27 pages and is illustrated by a number of facsimiles of original documents which add greatly to its interest. The Heath Clark series of lectures of the London School of

Hygiene and Tropical Medicine has already been fortunate in its excursion into malaria with the production of L. W. HACKETT's fascinating book *Malaria in Europe* [this *Bulletin*, 1937, v. 34, 446] and it may now be considered doubly fortunate with Russell's masterly review.

G. Macdonald.

DAVEY, T. H. & LIGHTBODY, W. P. H. **The Control of Disease in the Tropics. A Handbook for Medical Practitioners.** pp. x + 408, 85 illustrations. 1956. London: H. K. Lewis & Co. Ltd., 136, Gower Street, W.C.1. [47s. 6d.]

In their preface the authors state that prevention and control of diseases in the tropics are dealt with only briefly in most text-books on tropical medicine, and that text-books on public health are largely urban in outlook. Information on problems of disease as they exist in under-developed rural areas which form the major part of the tropics is scattered about in various publications, and the authors state that their aim is " to bring together the more essential parts of this within the compass of a handbook of convenient size . . . no attempt has been made to produce a comprehensive volume dealing with every aspect of public health in the tropics ".

The diseases dealt with are those commonly encountered in the tropics, and they include, besides those conventionally classified as tropical, such cosmopolitan infections as typhoid fever, smallpox, cerebrospinal fever, tuberculosis and venereal diseases—all of major importance.

The grouping of the infections has been planned on the basis of modes of transmission, in broad groups relating to:— low standards of personal and public hygiene; proximity and contact infections; insect-borne infections; infections from lower animals. This scheme is logical and is in keeping with the subject of control, and it is not important that the helminthic diseases (for instance) are not all included in one group.

Each disease is discussed under headings arranged in regular order:— geographical distribution, the parasite, epidemiology, diagnosis and control. Cycles of transmission are illustrated throughout by clear and easy original diagrams, and occasionally by attractive line sketches. After the sections on specific infections there are illustrated chapters on welfare services, village housing, food and vital statistics, and there is an Appendix of 12 sections on such useful information as the recognition of snails, examination of rats and fleas, and other practical matters. The index is satisfactory.

The information given is accurate, the language is clear and concise, and the tone sufficiently dogmatic: students will find it invaluable and it will be indispensable for public health officers in the tropics. The layout and printing attract the eye.

With the African scene particularly in mind the reviewer feels that more attention could have been paid to the special problems of industrial

development. Admittedly the specific problems of mines, factories and plantations, involving questions of the relevant industrial diseases, poisonings and accidents in addition to the questions of heat and ventilation, would require lengthy treatment, and have already been discussed in many special text-books, and could therefore hardly be adequately discussed in a short space. But tropical industry is already profoundly affecting the patterns of rural life, and the prevention of disease in migrant labourers and in the families they leave behind is becoming increasingly a problem which has important psychological and physical repercussions.

There is also another side to preventive work, which takes its origin from the demands of the people themselves for better living conditions, and this side may be fostered by judicious education in health matters and in social amenities. Health education is a difficult and inexact subject, but it has its importance, and could be amplified here.

Otherwise there is little to criticize. The general orientation of the book is towards the expert, who takes certain precautions and uses special techniques to prevent disease or to control it if it occurs. The reviewer welcomes it without reserve; it will undoubtedly take its place as an equal among the other distinguished publications which have come from the Liverpool School of Tropical Medicine. *Charles Wilcocks*

Reynes, V. Précis d'épidémiologie et prophylaxie des grandes endémies tropicales. [**Précis of Epidemiology and Control of the Major Tropical Endemic Diseases**] Preface by Vaucel. 3rd Edition (revised and augmented). pp. vii + 418, 57 figs. 1955. Paris VI^{e}: Masson & Cie, 120, Boulevard Saint-Germain. [2,800 fr.]

The book starts with an account of the cycle of transmission of disease and the various factors which may influence it, including here an analysis of the role of arthropods and leading to a summary of epidemic and endemic factors and mechanisms of control. Diseases are then handled in sections according to the means of transmission: the droplet infections, the faecal infections, those carried by arthropods, the helminthiases, and separately, tuberculosis, leprosy and beri-beri. In each of these the appropriate diseases are described on a framework which may be illustrated by that of malaria: there is description of the parasite, of the reservoir in man and the features of endemicity, the vector mosquitoes and their biology, susceptibility and immunity in man, epidemic and endemic features of the disease and prevention by mosquito control and drug prophylaxis. In this way all the main tropical diseases are discussed, including many cosmopolitan ones such as the pneumococcal and meningococcal infections, poliomyelitis and tuberculosis.

The reader can gain a picture of the communal aspects of disease and the general principles of control which is put unusually clearly and briefly,

and he can therefore understand the happenings in tropical hygiene. The book is however a précis, and although gaining an understanding the reader will not acquire the detailed knowledge necessary to implement a programme of control, for which other and more specialized works must be consulted. Within its scope it is excellent. *G. Macdonald*

RODENWALDT, Ernst. [Edited by.] **Welt-Seuchen-Atlas.** [World-Atlas of Epidemic Diseases] Part II. 2nd issue. pp. II/1–II/4, II/19–II/24, II/79–II/84, II/101–II/106, II/123–II/126, II/141–II/146, II/157–II/162, 3 text figs. & 10 folding pp. of coloured maps. [1955.] Hamburg 1: Falk-Verlag, Burchardstrasse 8. [In German & English.]

[This review also appears in the *Bulletin of Hygiene*, 1956, v. 31, June.]

The present issue continues the two previously published [this *Bulletin*, 1953, v. 50, 772; 1955, v. 52, 499], in substantially the same form. The text and maps deal with paratyphoid A in Europe 1900–1950 by BADER, the development of diphtheria in central Europe 1922–1952 by KANTER, dengue epidemics in the Mediterranean 1800–1950 by ULMANN, yellow fever in Africa 1939–1952 by HÖRING and HÖRING, trench fever in Europe 1914–1945 by BORMANN, leishmaniasis in Africa 1906–1952 by PIEKARSKI and SIBBING, filariasis in Africa 1939–1952 by EHRHARDT and WELLENSIEK, and the distribution of population in the Mediterranean area and in Africa 1950 by BURGDÖRFER. For each of these subjects there are one or more large excellently produced multicoloured maps illustrating the distribution, usually several smaller monochrome maps, and a lengthy written account covering epidemiology and distribution, with a bibliography. Some of these are examples of the great superiority of visual demonstrations over the written records. The two major maps recording the distribution of population give at a glance information both of the general and of the detailed local position which could not be transmitted in any other way. They are supplemented by a statement dealing largely with sources of information and degrees of reliability, and a tabulated record of statistics which together with the other material makes the information virtually complete. The map illustrating the distribution of leishmaniasis is clear, conveys a correct immediate impression of the situation and provides a source from which details can be sought in the excellent bibliography. The map on yellow fever together with its associated tables, is perhaps the best available illustration of the distribution of immunity to that disease. The maps on trench fever bring much that was new to the reviewer, and give a clear idea of endemic and epidemic distribution. Those of diphtheria in Europe give an excellent impression of the happenings leading to the present recession of the disease, though the smaller maps are perhaps more informative than the large.

In their own ways all of these accounts are good and the reviewer makes

no distinction between them in relation to the quality of the work which has gone into them, but only in the suitability of the visual form of presentation which is adopted. This turns on the number of records available (without many records reproduction on a large scale map gives a false sense of accuracy), on the number of factors to be illustrated (the optimum is very few), and whether it is intended that distribution in both space and time should be illustrated. It is not appropriate that the multitudinous data on population and the extremely few records of dengue outbreaks should be illustrated on maps of comparable scale, and the map of dengue loses by its very size. The greatest difficulty, due to the need to illustrate several points, has been met in the map on filariasis in Africa where the distribution of 7 species is recorded. The author and editors have made a good compromise by the presentation of a map from which the species prevalent in any area can be seen quite easily, but conversely it is difficult to see the general distribution of any one species. For two of them, *Loa loa* and *Acanthocheilonema* [*Dipetalonema*] *perstans*, this is shown in small supplementary monochrome maps which are examples of clarity and ease in conducting the reader to original sources in the bibliography. The editors are still uncertain as to the best way of showing distributions of incidence in time on a map which also shows variations in space, and still experiment with the superimposition of dates, the use of symbolized gradients, variations in hatching, and the use of contrasting maps for different dates. The last seems much the most successful and demands no more than small, simple monochrome maps. Second to this method, the symbolized gradient gives a not unreasonable impression of happenings, but the reviewer has the greatest difficulty in following superimposed dates or methods of alternative hatching to record time happenings. The authors and editors are struggling to establish a technique and with progressive success which makes their series a valuable one.

[The reviewer takes this opportunity of correcting a misstatement in his previous review and points out that it was through his and not the author's oversight that he failed to trace the background for some of the points shown on the map dealing with bacillary [Shiga] dysentery in Africa, and regrets that he should have misled readers.]

G. Macdonald

Printed in Great Britain under the authority of Her Majesty's Stationery Office
by The Eastern Press, Ltd., London and Reading.

(2106) Wt. P8523/477 6/56 E.P. Ltd. Gp. 566.